ANNALS OF
INTERNAL MEDICINE

VOLUME 19 DECEMBER, 1943 NUMBER 6

THIOCYANATE GOITER IN MAN*

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THAT a definite relationship exists between iodine deficiency and many non-toxic goiters is well established. Indeed endemic goiter is usually, and perhaps too readily, accepted as being due to iodine deficiency. Experimentally, thyroid hyperplasia has been produced in various laboratory animals by many goitrogenic agents other than iodine deficient diets. Astwood, et al.[1] in a recent report, referred to extensive literature on a variety of goitrogens.

Some of the most interesting studies in goitrogenesis were incited by observations made by Chesney, Clawson and Webster [2, 3, 4] in 1928. They observed large hyperplastic goiters in rabbits maintained on cabbage diets. In spite of the fact that these thyroids showed extreme hyperplasia, the animals were found to have low metabolic rates. Though the goiters could be prevented by administering iodine, if iodine was given after the goiter had developed, a severe thyrotoxicosis ensued promptly. Marine, Baumann, Spence and Cipra [5] confirmed this work and also found that the leaves of many brassica plants contained some goitrogenic agent. Since it had been reported that certain nitrile compounds had been isolated from the leaves of several brassicae, Marine [5, 6, 7, 8] and his associates investigated the action of several cyanide compounds on the thyroids of laboratory animals. They observed that methyl cyanide, and several of the other nitriles, produced marked thyroid hyperplasia with low metabolic rates and exophthalmos. Hertz and Roberts [9] have used potassium thiocyanate to produce thyroid hyperplasia. Astwood [10] has also produced thyroid hyperplasia in animals treated with potassium thiocyanate.

* Received for publication May 19, 1943.
From the Thyroid Clinic of the Massachusetts General Hospital. Aided in part by grants from the John and Mary R. Markle Foundation, the H. N. C. Gift and Proctor Fund, Harvard University. Read in preliminary form at the meeting of the American Society for Clinical Investigation in Atlantic City, May 4, 1942.

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Kennedy and Purves [11] have recently reported that rape seed as well as the seed of other brassica plants when fed to rats produce large hyperplastic goiters. Sharpless [12] and his associates have reported that soy bean flour when fed to rats has a strongly goitrogenic action. These soy bean goiters could be prevented by the administration of iodine.

Another group of very interesting and important goitrogens has recently been reported by three different groups of workers. The MacKenzies [13] observed large goiters in animals being treated with sulfaguanidine. At about the same time Richter and Clisby [14] reported their observations of large hyperplastic goiters in animals receiving thiocarbamide. Recently the MacKenzies [15] working in one laboratory and Astwood [1, 10] and his associates in another, have found goitrogenic activity in various other sulfonamides and in molecular compounds similar to thiourea. It was observed, in fact, that most of the sulfonamides are goitrogens as also are many thiourea-like compounds. It is of real importance to note that it was not possible to prevent the action of such goitrogens by means of iodine. Thyroxine, on the other hand, did prevent the goitrogenic action of these drugs. Astwood [10] had previously observed that iodine would prevent the development of goiters in animals treated with potassium thiocyanate.

With the advocated use of soy beans in the modern diet, the liberal prescribing of the sulfonamides in clinical medicine, and with widespread use of thiocyanate in treating hypertension, it becomes of practical importance to know whether such agents have any goitrogenic action in man. It is also of theoretical importance, and of academic interest, to learn as much as possible about thyroid physiology by determining with available tools what we can about the mechanism of such goitrogenesis.

The present report deals with observations made on two patients who developed goiters while receiving potassium thiocyanate for treatment of hypertension. A third case of similar sort was seen in consultation with Drs. R. S. Palmer and D. Kinsey. In this last-mentioned case, that of a woman of 45 years with severe hypertension, a goiter developed after prolonged thiocyanate treatment and disappeared on stopping the drug. It had not redeveloped on resumption of the drug up to September 8, 1943. Barker [16] has also observed goiters develop in a few hypertensive patients being treated with potassium sulfocyanate. His patients had decreased basal metabolic rates and were observed to improve with thyroid therapy even though the drug was continued. The goiters disappeared and the metabolic rates returned to normal. Fahlund [17] has recently reported a case of painful swelling of the thyroid in a patient receiving thiocyanate therapeutically. The swelling and pain disappeared promptly when the drug was stopped. Kobacker [18] has also observed a goiter develop in a patient receiving this drug in treatment of hypertension, as have also Foulger and Rose.[19] Kobacker's case developed myxedema also. The goiter and myxedema disappeared when the drug was stopped but returned when this therapy was resumed. Though the evidence for cabbage and thiocyanate

goiters being on the basis of identical mechanisms is lacking, it is of interest to refer to Suk's [20] report of large goiters occurring endemically in a central European community where cabbage is a principal dietary item.

Case Reports

Case 1. Mr. R. D., a 35-year-old white W.P.A. laborer, entered the medical out-patient clinic of the Massachusetts General Hospital on June 24, 1940, complaining of headaches and of ankle edema. He gave a history of nephritis nine years previously. For three months prior to admission he had been dyspneic and had had pedal edema. He had had severe headaches for three weeks previous to admission. Examination revealed moderate hypertension with some enlargement of the heart to the left. A systolic murmur was heard at the apex. A few râles were heard in both bases. The thyroid was not enlarged. Some nicking of the retinal vessels was observed. During a three month period of symptomatic treatment his blood pressure varied between 190 mm. Hg systolic and 110 mm. diastolic and 220 mm. systolic and 130 mm. diastolic. The headaches persisted.

On September 19, 1940, he was instructed to take potassium sulfocyanate in syrup of wild cherry. The daily dosage of potassium thiocyanate varied between 0.15 gm. and 0.45 gm. The blood cyanate levels during the period of treatment averaged 5.8 mg. per cent. The highest blood level recorded was 8.3 mg. per cent. While taking the thiocyanate, his symptoms improved and the blood pressure fell to 130 mm. Hg systolic and 110 mm. diastolic.

One year after beginning the thiocyanate treatment the patient returned to the clinic complaining of a painless swelling in his neck and of some swelling of his eyes. He entered the hospital on October 7, 1941. On closer questioning the patient admitted that for several months he had had some intolerance to cold and easy fatigue. He also reported a loss of libido. The patient's wife reported that she had observed some dulling of the patient's sensorium. The neck swelling was found to be a very hard diffusely enlarged thyroid which was estimated to be 8 to 10 times the normal size. It was hard enough strongly to suggest malignancy. A loud bruit was heard over it. Moderate exophthalmos with a bilateral lid lag was readily demonstrated. No tremor was present.

The basal metabolic rate was found to be minus 17. Plasma protein iodine was reported as 2.7 gamma per cent. In our laboratory this level of plasma iodine is within the range of levels observed in myxedematous patients.

The ability of the thyroid to collect iodine was determined by means of the radioactive iodine technic of Hertz and Roberts.* Of a dose of 1.0 mg. of radio-iodine given October 15, 20 per cent was excreted in the urine in the first 24 hours, and 6 per cent in the second. The total excretion was, therefore, approximately 30 per cent, which is in the range found by Hertz and Roberts in classic Graves' disease, and is less than that of normal persons.

The urine was studied for substances which might stimulate the thyroid. No such material could be found in an acetone precipitate of the urine. An aliquot of the same 24-hour specimen of urine which had been autoclaved before extraction, however, contained about twice as much thyrotropic substance as is usually demonstrated in the urine of normal persons treated in the same manner.

Under local anesthesia a biopsy of the goiter was done. At this operation the thyroid was found to be extremely vascular. Microscopic examination of the biopsy specimen revealed an extremely hyperplastic thyroid with marked papillary overgrowth. The material bore a striking resemblance to that of goiters which Hertz

*We are indebted to the Physics Dept. Massachusetts Institute of Technology for this determination.

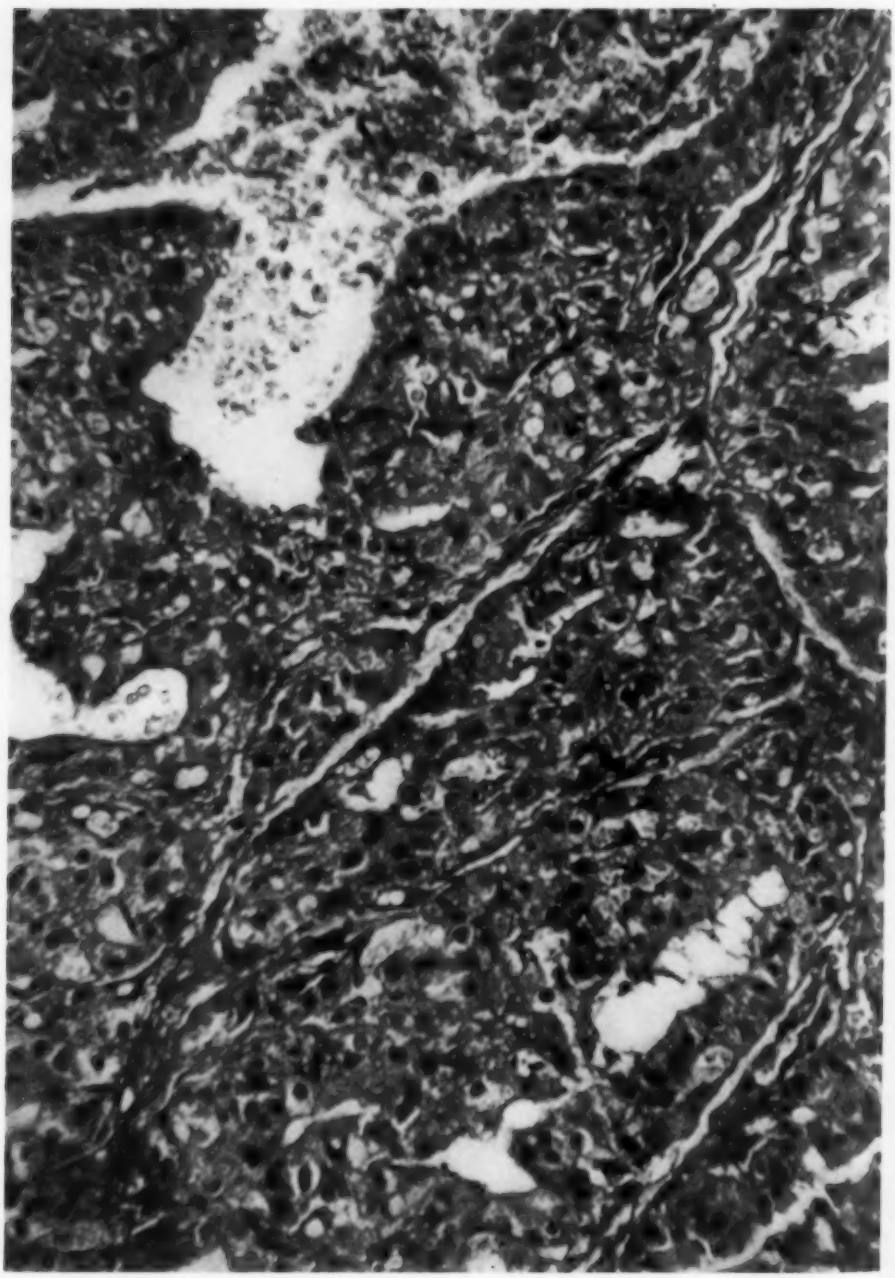

FIG. 1 A. Photomicrograph of thyroid tissue removed at biopsy in Case 1. × 400 diameters.

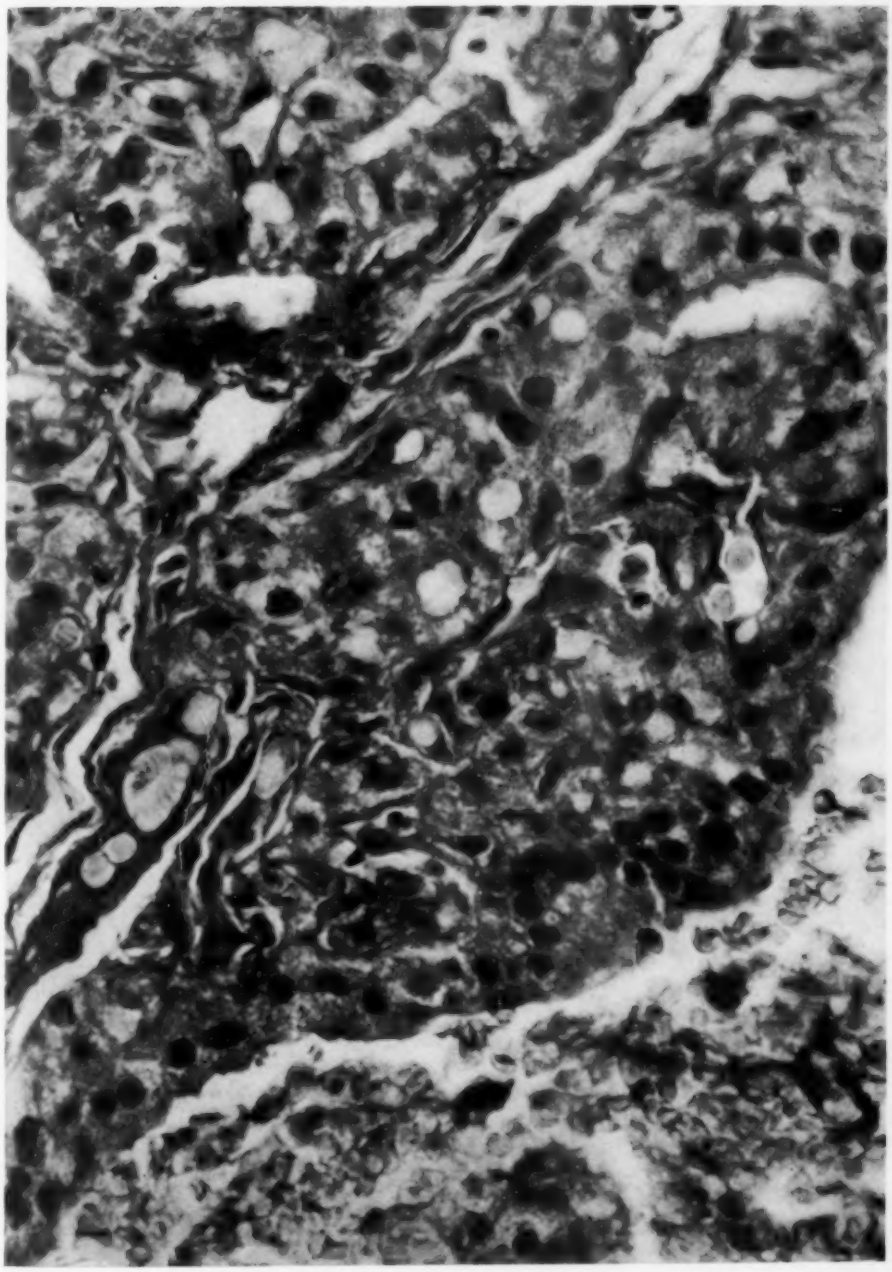

FIG. 1 B. Photomicrograph of thyroid tissue removed at biopsy in Case 1. × 900 diameters.

and Roberts [9] had previously produced in rabbits by the administration of thiocyanate (a report of these studies will be published elsewhere). An explant of the biopsied tissue exposed to thyroid stimulating hormone with tissue culture technics was found to inactivate all of the thyroid stimulating hormone (TSH) in the bathing medium. This inactivation is similar to that observed when thyroid tissue removed from patients with Graves' disease is exposed to TSH in a similar manner, and probably explains our inability to demonstrate any active thyroid stimulating hormone in the unautoclaved urine.

The thiocyanate was stopped. Ten days after stopping the drug the basal metabolic rate had risen to plus 5 and the patient reported that he felt much less fatigued. He also reported that he had a better tolerance for cold. Within three weeks after stopping the drug, the thyroid had regressed in rather remarkable fashion to approximately normal size and the plasma iodine had risen to a normal level. The exophthalmos was less noticeable but the lid lag persisted.

Three months after the medication was stopped the patient returned to the clinic complaining of frequent severe headaches. The blood pressure had risen to 180 mm. Hg systolic and 120 mm. diastolic. Again he was instructed to take potassium thiocyanate in doses of 0.3 gm. daily. He was followed carefully with close observation of his thyroid symptoms, frequent metabolic rates, and with plasma protein iodines. One month after resuming the thiocyanate therapy, the plasma iodine was found to have fallen to a myxedematous level and remained at that level until the drug was stopped. Six weeks after resuming the drug, the patient complained of excessive fatigue, intolerance to cold and of a loss of libido. The lid lag persisted and the exophthalmos became more definite. The thyroid also began to increase in size. These symptoms and findings persisted until the drug was stopped again at the end of nine weeks, at which time the thyroid was estimated to be three times the normal size. No bruit was audible. During this period of observation the basal metabolic rate did not fall below normal. Ten days after the drug was stopped, the plasma iodine had returned to a normal level. The patient reported that he was free of fatigue and that he had a better tolerance for cold. He also reported a return of libido. The lid lag remained.

The patient continued without any thiocyanate therapy for a period of three months. He felt well for most of this time and was free of the headaches which originally had been his primary complaint. His blood pressure began to rise gradually and finally reached a level which previously had produced headaches, i.e., 174 mm. Hg. systolic and 104 mm. diastolic. He then was instructed to take KSCN in syrup of wild cherry. The dose of KSCN was 0.3 gm. daily. He was also instructed to take U.S.P. thyroid 0.1 gm. daily. The blood pressure was lowered again to a level of 142 mm. Hg systolic and 92 mm. diastolic. While taking 0.1 gm. daily of U.S.P. thyroid with the same amount of KSCN as previously he had the desired beneficial effect on his hypertension without developing the signs suggestive of hypothyroidism observed with the previous trial with this drug. Four months after starting the drug, with the onset of cold weather he did complain of some intolerance to cold and of an increased need for sleep as well as of loss of libido. The dose of thyroid prescribed was increased to 0.2 gm. daily. He continued to take the thiocyanate and the thyroid 0.2 gm. daily. On such a régime he has continued to get the desired effect on his hypertension and has remained free of hypothyroid symptoms.

Case 2. Mrs. D., a 34-year-old white American housewife, was admitted to the medical wards of the Massachusetts General Hospital for study of hypertension.

The patient had gone through an uneventful childhood with the exception of migraine headaches which began at the age of 11. She gave no history of scarlet fever, prolonged or recurrent sore throats, or any other debilitating illness. She had first been told that she had hypertension by her family physician at the age of 18, 16 years before entry.

Eight years before admission for study, in 1933, the patient became pregnant for the first time. After the third month of pregnancy she was found to have albumin in the urine, and her blood pressure was said to be rising. Labor was induced in the seventh month. She was delivered of a live child and had a normal recovery. Her blood pressure returned to normal. He second pregnancy followed two years later. This pregnancy likewise was associated with albuminuria and an increase in blood pressure. Again labor was induced in the seventh month and a live child was de-

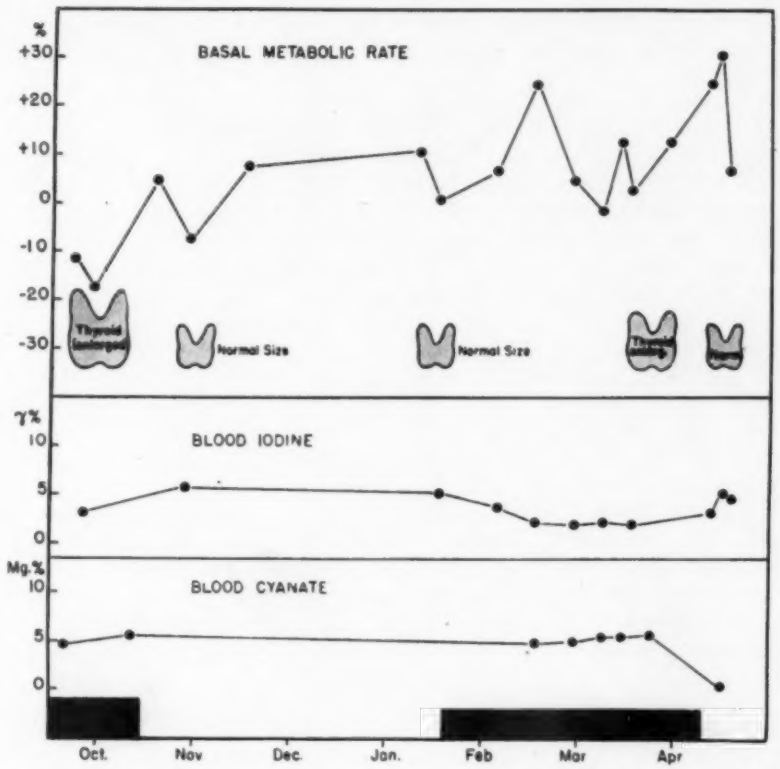

FIG. 2. Basal metabolic rate, blood iodine level, blood cyanatic level and thyroid size in Case 1. The left-hand black rectangle denotes administration of 0.45 gm. of potassium thiocyanate daily; the right-hand rectangle 0.3 gm. daily.

livered. The blood pressure again returned to normal following delivery. The third pregnancy was normal, and was terminated with the normal delivery of a full term baby.

The fourth pregnancy was terminated in the eighth month with a Caesarian section because of signs of severe toxemia associated with hypertension. This delivery was followed by phlebitis. The blood pressure following this pregnancy did not return to normal and the patient continued to show a slight trace of albumin. She was referred to the Massachusetts General Hospital for consideration of surgical treatment of her hypertension.

The inventory by systems revealed a history of pleurisy two years previously and a story of exertional urinary incontinence.

Physical examination showed a rather pale, well developed white woman. The fundi showed slight sclerosis of the retinal vessels. The heart was slightly enlarged

in the region of the left ventricle by physical examination and this was verified by roentgenographic examination. There was a soft systolic murmur heard at the apex. The blood pressure was 150 mm. Hg systolic and 100 mm. diastolic. The left leg was found to be swollen and edematous. The thyroid was described as of normal size.

Her blood pressure was found to be labile by the cold pressor test, the sedative test and with postural changes. She concentrated urine to 1.020. She excreted phenolsulphonphthalein 30 per cent in 15 minutes and 73 per cent in two hours.

Because of subsiding thrombophlebitis it was decided to postpone operative treatment for six months. She was discharged from the hospital to be followed in the hypertension clinic.

Three months later she returned to the medical clinic complaining of rather severe and frequent headaches. Her blood pressure at that time was found to be 180 mm. Hg systolic and 120 mm. diastolic. She was instructed to take potassium sulfocyanate 0.3 gm. daily in syrup of wild cherry. Blood levels of sulfocyanate never were observed to exceed 4.7 mg. per cent. Her blood pressure fell to 130 mm. Hg systolic and 80 mm. diastolic. Four months after starting to take the thiocyanate the patient returned to the medical clinic complaining of feeling tired and slowed down. She was found to have a diffusely enlarged thyroid which was estimated to be about three times the normal size. It was firm and smooth. No bruit was heard. No eye signs were observed. The thiocyanate was stopped and the patient was readmitted to the hospital for study two weeks later.

When the patient was admitted to the hospital, she was found to have a goiter as described in the Out Patient Department. She reported that this had been present for about six weeks. She denied any intolerance for the cold but did report that she had gained 22 pounds of weight since her discharge from the hospital eight months previously. Her metabolic rate upon admission to the hospital was found to be minus 12. She was again given KSCN 0.3 gm. daily. Her metabolic rate fell within 12 days to minus 32. The goiter, however, did not get larger. Indeed, it was the opinion of the service that it had grown somewhat smaller. Her blood pressure while in the house varied between 132 mm. Hg systolic and 90 mm. diastolic, and 120 mm. systolic and 88 mm. diastolic. The blood cholesterol was not elevated. It was reported as 179 mg. per cent. The plasma iodine was determined by Dr. W. T. Salter at Yale School of Medicine and was reported by him to be 2.8 gamma per cent. This level is within the range observed in patients with myxedema.

In this case also a search was made for thyroid stimulating properties in the urine. None, however, could be demonstrated in an acetone precipitate. However, as in Case 1, when an equal aliquot of the same urine was autoclaved, about twice as much thyrotropic activity developed as is usually found in the autoclaved urine of normal people. Unfortunately the patient would not consent to a biopsy of the thyroid.

The patient was discharged with instructions to continue taking the thiocyanate and to be followed in the thyroid clinic.

In the out-patient department the basal metabolic rate was found to have risen to minus 15 where it remained. The patient presented the picture of a myxedematous individual. The thyroid remained about twice the normal size. No eye signs were observed. Two months after her discharge from the hospital, she was instructed to continue with the thiocyanate therapy and to take U.S.P. thyroid 0.1 and 0.2 gm. on alternate days. After thyroid was added to her régime, the metabolic rate rose to minus 6 and her thyroid returned to normal size within two months. The picture of myxedema disappeared. The blood pressure remained at a satisfactory low level of 114 mm. Hg systolic and 74 mm. diastolic.

Discussion

We are aware that any assumption that experimental cabbage goiters, brassica seed goiters and cyanide goiters are on the basis of the same mechanism as are the goiters that we have observed in thiocyanate treated patients, is an apriority. However, if we compare the observations made on these two patients with those made on animals treated with agents which are thought to be similar, we may formulate certain hypotheses as to the mechanism of such goitrogenesis.

Our observations may be epitomized as follows. We have observed goiters develop in two patients who were receiving potassium thiocyanate for treatment of hypertension. These goiters were associated with decreased thyroid function as evidenced by clinical symptoms of hypothyroidism, low basal metabolic rates, and plasma protein iodine levels of the sort usually observed in patients having myxedema. Histological examination of biopsy material removed from one of these patients revealed an extreme hyperplasia of the thyroid. One patient developed exophthalmos with lid lag. In one patient the goiter, as well as the clinical and laboratory evidences of hypothyroidism, disappeared when the thiocyanate administration was stopped, but returned when the drug was taken again. In both cases the goiters and clinical signs of hypothyroidism disappeared when thyroid was administered though the administration of thiocyanate was continued.

Webster and Chesney [4] and Marine [5] and associates found that they could prevent the development of goiters in animals receiving a cabbage diet or methyl cyanide if thyroid or iodine were administered at the same time. The former investigators also reported that if iodine were administered to animals with large cabbage goiters, the picture changed from that of myxedema to that of severe thyrotoxicosis, which in some instances was fatal. The observed decreased amount of labeled iodine excreted in the urine of our first patient probably indicates an increased avidity of this type of goiterous tissue for iodine. A hunger for iodine of this degree is seen as a rule only in untreated classic thyrotoxic patients. The above phenomenon described by the Baltimore investigators is probably on the same basis as is this observed increased uptake of iodine by the cyanate goiterous tissue. Griesbach, Kennedy and Purves [21, 22] reported that the pituitaries of animals having goiters produced by a brassica seed diet presented histological changes similar to those observed in the pituitaries of thyroidectomized animals. They also reported that goiters could not be produced in hypophysectomized animals fed the same diet.

It would seem then, that the thyroid hyperplasia is secondary to an increased secretion of the thyroid stimulating hormone of the pituitary (TSH). No free active TSH was demonstrable in the urine of our patients. We feel that this is due to an inactivation of the pituitary hormone by the hyperplastic thyroid tissue. This is evidenced by our observation that explants of the biopsy tissue taken from our first patient's goiter inactivated as much

TSH exposed to the tissue in bathing medium as does the thyroid tissue of Graves' disease.[23] The thyrotropic effect of urine which had been autoclaved before extraction was very definite and amounted to about two times that observed in the autoclaved urine of normal human beings. We interpret this observation as a reactivation of TSH which had been inactivated by the thyroid cells. (The reactivation of TSH will be discussed in a subsequent communication.) These observations would indicate that there is an increased activity of the pituitary in states of thiocyanate goiter. Such increased pituitary activity is probably due to an induced hypothyroidism.

There are various theories to explain the action of these agents in producing the hypothyroid state. Marine [24] and associates suggested that the agents used by them interfered with the action of the thyroid hormone by disrupting the cellular oxidation systems of tissue cells, in other words, an end organ effect, and thereby produced a lowered metabolism of the entire organism. Williams and Bissell [25] also adhere to this interpretation. It was postulated that such a lowered metabolism would stimulate the pituitary via the hypothalamus, to secrete an increased amount of TSH. This explanation seems untenable because of our own observations, and because of those reported by Barker [16] that the goiters and symptoms of lowered metabolism disappeared when thyroid was administered, although the thiocyanate therapy was continued. Dr. J. Lerman [26] has made an isolated observation that also is in disagreement with Marine's theory. He administered potassium thiocyanate to a controlled myxedematous patient who was receiving a standard dose of U. S. P. thyroid. The thiocyanate did not cause any fall in the basal metabolic rate.

The low levels of plasma iodine observed in our patients indicate decreased circulating thyroid hormone and should direct our attention to some interference with the formation of normal thyroid hormone as a possible explanation for the induced hypothyroidism. These low levels of plasma iodine constitute further evidence against the theory that end-organ sensitivity is reduced by cyanate. Were end-organ sensitivity reduced, the plasma iodine reflecting as it does, thyroid hormone level, should be increased. The experimental observations that goiters cannot be produced in laboratory animals with potassium thiocyanate nor with the other similar goitrogens if iodine is administered suggest that the decrease in circulating thyroid hormone is due to some interference with normal iodine metabolism. This interference with iodine metabolism might be due simply to a diversion from the thyroid of exogenous iodine by this group of goitrogens. Supposing such an action actually to be the mechanism, then it can be further supposed that iodine, when administered in excess, will displace the goitrogen in a similar fashion.

Another possible explanation is that of a paralysis, or inactivation, of the enzyme systems, the functions of which are those of iodinating the thyroid hormone. Thus it would appear that a hypothyroid state would result from the secretion of a non-iodinated thyroid hormonal skeleton, i.e., thyronine or

a thyronine-like substance. The thyronine-like substance being non-iodinated would have no calorigenic action and would therefore permit the rate of metabolism to fall to the level of a thyroidectomized organism. The low metabolic rate would in turn cause stimulation of the pituitary to increase its secretion of thyroid stimulating hormone. The absence of the thyroid

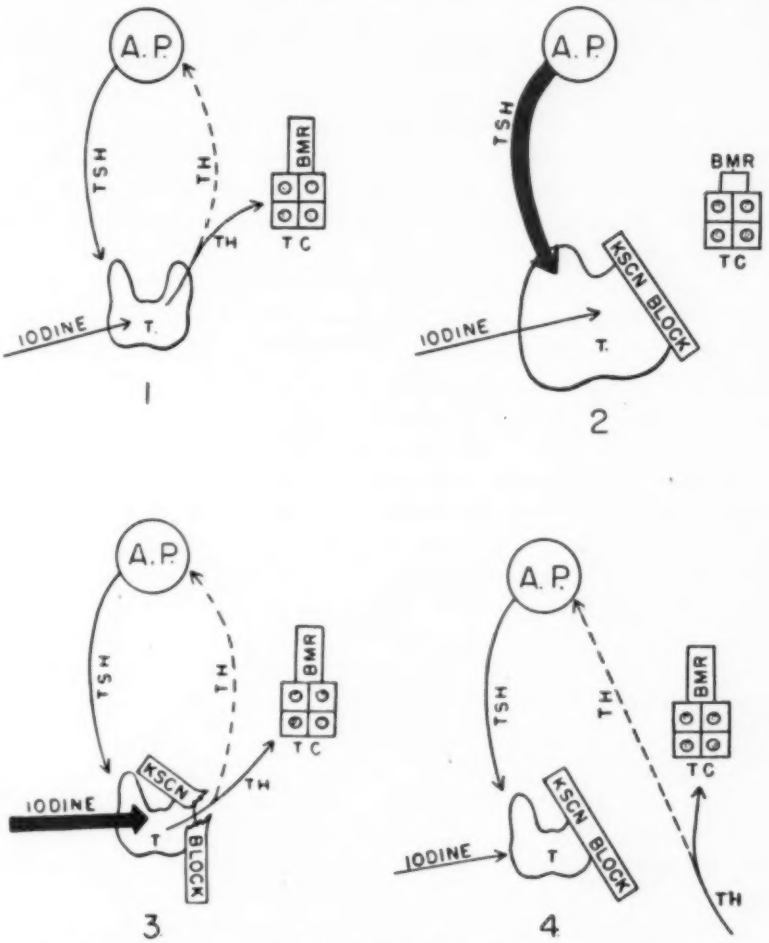

FIG. 3. Diagrammatic representation of the effect of cyanate on the pituitary-thyroid axis.

1. Normal relationships. The anterior pituitary—AP—by means of its hormone—TSH—and in the presence of an adequate supply of iodine, stimulates the thyroid—T—to produce its hormone—TH—which stimulates the metabolism of tissue cells—TC—and inhibits AP.

2. Cyanate imposes an obstruction to the completion of TH. The BMR of TC therefore falls, and the uninhibited AP produces an excess of TSH. This causes hyperplasia of T, but since the block remains, no active TH is delivered to the body.

3. The supply of an excess of iodine forces the cyanate block so that TH is made in adequate amounts, BMR remains normal and TSH formation remains normal, and therefore no enlargement of T takes place.

4. The supply of TH from without by-passes the cyanate block so that BMR remains normal and TSH formation remains normal, as does the thyroid gland.

hormone would permit the pituitary to elaborate the TSH without any inhibition. In response to the abnormal stimulation with TSH the thyroid would respond with a marked hyperplasia and would secrete increased amounts of non-iodinated thyroid protein (figure 3). The theory of the non-iodinated thyroid hormone could account for the experimental observation that laboratory animals having large cabbage goiters promptly develop severe thyrotoxicosis when iodine is administered. This theory seems tenable in the light of our present information and is compatible with the observations made in patients who developed goiters while taking thiocyanate therapeutically as well as with those observations on animals made goiterous by the administration of this group of agents. It is very likely that a greater knowledge of thyroid cellular physiology will permit the formulation of more elaborate, and no doubt more intelligent, theories as to the mechanism of the goitrogenesis of such agents.

The exophthalmos produced in rabbits treated with methyl cyanide by Marine [8, 24] and his associates gave rise to considerable speculation concerning the mechanism of exophthalmos. Because of observations made on similar exophthalmic animals after treatment with pituitary extracted thyrotropic hormone, they postulated that the exophthalmos as well as the thyroid hyperplasia was due to increased pituitary activity in secreting TSH. In view of the observations of Griesbach, Kennedy and Purves [21, 22] referred to above, it seems tenable that the exophthalmos is on the basis of increased pituitary activity. It is interesting that only one of our patients developed exophthalmos. Again we have the suggestion that the response of an organism to hormonal treatment or secretion is dependent on the state of the end-organ.

On the practical side one is entitled to ask why is thiocyanate goiter not more common in persons being treated with thiocyanate for hypertension? The answer that suggests itself, but that cannot be proved is that iodine occurring naturally in most environments is usually sufficient to prevent it. One is led to guess further that had thiocyanate been used widely in endemic goiter regions prior to the introduction of iodized salt there might have been considerable thiocyanate goiter.

In the field of therapeutics it can be pointed out that in the treatment of hypertension with thiocyanate over long periods of time the administration of prophylactic doses of iodine should prevent the development of thiocyanate goiter. Also when thiocyanate goiter has developed, it is not necessary to discontinue the administration of thiocyanate, which may be essential from the point of view of the blood pressure, it is merely necessary to give thyroid along with it. One can thus get the desirable effect of thiocyanate on the blood pressure and stop the undesirable effect upon the thyroid gland.

Summary

1. Two cases of thiocyanate goiter in man are reported. Note is made of a third seen in consultation. Several from the literature are cited.

2. Thiocyanate goiter is characterized by (a) hyperplasia of the thyroid; (b) symptoms of hypothyroidism; (c) exophthalmos (seen in one case); (d) low basal metabolic rate; (e) low blood iodine; (f) decreased urinary excretion of labeled iodine; (g) increased urinary excretion of thyrotropic hormone in the inactivated form.

3. The theory is advanced that this drug blocks the formation of thyroid hormone by the thyroid, and that the consequent lowering of concentration of active thyroid hormone in the blood stream causes stimulation of the anterior pituitary to produce an excess of thyrotropic hormone. This in turn causes thyroid hyperplasia but, because of the block, no increase in physiologically active thyroid hormone output. It is a hyperplasia of frustration. An excess of administered iodine may force the block, and cause liberation of active hormone. Administration of thyroid by-passes the block, and relieves the situation by substitution.

4. Thiocyanate goiter can probably be prevented by prophylactic doses of iodine.

5. Thiocyanate goiter can be relieved by the administration of thyroid even when thiocyanate administration for hypertension is continued.

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ACUTE LUPUS ERYTHEMATOSUS DISSEMINATUS *

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In comparatively recent years much attention has been given to the symptom-complex called acute lupus erythematosus disseminatus. The purpose of this paper is to present a concise review of the literature on this subject with emphasis on its clinical aspects.

Synonyms: Visceral erythema group (Osler [1]), disseminated lupus erythematosus, atypical verrucous endocarditis (Libman-Sacks [2]), fever of unknown origin (Christian [3]), and diffuse peripheral vascular disease (Baehr and others [4]).

Definition: Lupus erythematosus disseminatus acutus is a clinical entity even though the name emphasizes only one of several characteristic symptoms of the syndrome. It is a disease of unknown etiology associated with widespread visceral lesions predominantly involving the kidneys, lymph nodes, blood vessels, serous and endocardial surfaces, as well as the skin.

History: Kaposi [5] in 1872 first pointed out the acute disseminated form of lupus erythematosus. He also called attention to the fact that the chronic form can become acute. In 1895 Sir William Osler [6] reported under the name erythema exudativum multiforme a group of cases with polymorphic erythematous skin lesions associated with a variety of visceral lesions such as acute nephritis, gastrointestinal or urinary bleeding and splenomegaly, endocarditis and pericarditis. Osler's case number 19, with lesions of lupus erythematosus and erysipelas-like eruption (Kaposi's erysipelas perstans faciei) and number 26, with lupus erythematosus lesions, both of whom died with evidences of nephritis, were probably identical with, or variants of, acute disseminated lupus erythematosus. Fordyce [7] in 1899 first described the capillary thrombosis and the aggravating effect of frost bite and sunburn on the lesions. In 1911 Libman first recognized the existence of a peculiar clinicopathologic entity, which he and Sacks reported in 1924 [2] as a "hitherto undescribed form of valvular and mitral endocarditis" or "atypical verrucous endocarditis." They went on to say that "it is not improbable that a certain relationship exists between the atypical form of endocarditis and certain of these cases included in the erythema group." Keefer and Felty [8] reported three fatal cases of acute disseminated lupus erythematosus with autopsy of two in 1924. Since these early reports an ever increasing number of cases have been, and are being, reported in the literature because a clinical entity has been established.

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Incidence: The disease is not common, but most of the larger hospitals have had several cases at one time or another. It occurs most frequently among peoples living in the northern climates (Kierland [9]).

Race: The white race seems more susceptible to the disease. However, two of the three cases reported by Keefer and Felty [8] were negroes.

Sex: There is a marked predilection for females. Kierland [9] finds that 77 per cent of the acute lupus erythematosus disseminatus cases are in women. A few cases have been reported in males. Rose and Pillsbury [10] in their study of 12 cases found three cases that were males. Baehr [4] et al. reported only one male in their series of 23 cases.

Ginzler and Fox [11] reported a case of acute lupus in a 17 year old male of Anglo-Scotch birth. One of Madden's [12] five cases was a male.

Age: Steward and Goeckerman,[13] after a careful search in the literature up to 1931, found only four cases under 15 years of age. Madden [12] in 1932 reported a case in a boy five years of age; "the patient was exhibited at an annual meeting of the Minnesota Dermatological Society, and the diagnosis was concurred in by all the members present." The average age group is in the second or third decade, most frequently about 25 years of age.

Duration: The duration is quite variable because death is usually due to complications. It ranges from a few weeks to several years, the average duration being 18 months. Reifenstein et al.[14] in their report of 17 cases found no demonstrable correlation of duration with severity and extent of pathologic lesions. Some of the most severe lesions occurred in cases in which the clinical course could not be traced back farther than a few months.

The mortality of the disease is high; more than 90 per cent of cases end fatally within five years. A striking characteristic is the tendency for acute cutaneous and systemic manifestations to appear or recur after exposure to sun or ultraviolet light, roentgen-rays, cold, or the intracutaneous injection of irritating substances such as tuberculin.

General Characteristics: Acute lupus erythematosus disseminatus is characterized by all or many of the following features: erythematous cutaneous lesions, polyarthritis, prolonged fever, leukopenia with secondary anemia, polyserositis, endocarditis, nephritis and a remittent cachectic course, with a fatal termination weeks to several years after the onset.

The clinical course is extremely variable, since termination is usually the result of some complication. A patient who is apparently moribund may occasionally improve to such a degree that he or she may be discharged from the hospital as cured, only to return weeks or months later and go rapidly to exitus. On the other hand, a patient may have a small erythematous lesion which will initiate a fulminating and rapidly fatal illness. The clinical picture may be preceded by arthralgia, malaise, recurrent bouts of fever or other vague symptoms of ill-health over a prolonged period. Sometimes there is a history of seasonal bouts of skin lesions occurring in the summer after undue exposure to the sun.

Skin Lesions: The butterfly distribution of the skin lesions is a description that was, at one time, overemphasized. The distribution and sequence of involvement of the skin areas vary somewhat; however, the usual sequence is face, neck, hands, extremities and trunk. The moist surfaces, including the labia majora may become involved and present distressing symptoms (Madden's case 2 [12]). At times the skin lesions may closely imitate those occurring in acute pellagra, erysipelas and erythema multiforme (Weidman and Gilman [15]).

The eruption begins as erythematous patches which tend to coalesce and cover a large area. The lesions are clearly demarcated, dusky red, and have a bluish tinge. The erythema is essentially fixed whereas that seen in erysipelas is migratory. Baehr [4] noted also that the erythema is characteristically located on the ends of the fingers, around the nail beds, on the thenar and hypothenar eminences, and occasionally on the ends of the toes and the ball of the foot. The follicular orifices are dilated and often plugged. As atrophy ensues there appears a fine, gray, firmly adherent scale. Depending upon the amount of edema, the lesions may become papular, vesicular or bullous. When the superficial vessels become thrombotic or their walls injured by trauma, hemorrhagic lesions in the form of purpura-like macules, vesicles and bullae occur. At the height of the disease, the patients often show erythematous or petechial areas on the mucous membranes, particularly the mouth. These soon develop into small ulcers surrounded by an erythematous or hemorrhagic areola. They are prone to ulcerate and discharge purulent material. Marked pigmentation of the face is common during remission, and diffuse alopecia is the rule (Belote [16]).

Most dermatologists divide the lesions of lupus erythematosus roughly into two groups, the chronic discoid form and the acute disseminated variety.

The chronic or discoid form of lupus erythematosus is generally recognized as of slow growth and commonly associated with a good prognosis as far as life is concerned. However, it occasionally disseminates as result of overexposure to sunlight or gold therapy; and when it does, it takes on the same characteristics as the acute form. Stokes [17] warns that when the eruption of chronic lupus erythematosus begins to spread from the face to other parts, or to be associated with marked involvement of the mucous membranes, disseminated lupus erythematosus impends. He describes such an occurrence in a 39 year old white man who had had the chronic form for two years. Belote [16] considers the acute and chronic types as manifestations of the same disease.

O'Leary [18] subdivides the acute disseminated variety into: (a) generalized discoid or chronic disseminate, (b) subacute disseminate, (c) acute disseminate. Distinction between the subacute and acute is relative and depends on the severity and duration of the skin lesions and systemic symptoms.

The skin lesions in all types of lupus erythematosus are described as being painless. Mild itching or burning are usually the only cutaneous subjective symptoms which may occur during periods of increased activity (Kierland [9]).

The question often arises as to whether the visceral lesions of the acute disseminated lupus erythematosus syndrome may exist in the complete absence of cutaneous lesions. Baehr,[4] Libman and Sacks,[2] Friedberg,[19] and Tremaine [20] report cases in which the skin lesions appeared some months after the clinical symptoms.

Arthritis: Arthralgia is usually present at one time or another. It may precede or accompany the skin lesions and systemic phases of the disease. Slocumb [21] found the incidence of joint involvement in the chronic disseminated, subacute disseminated and acute disseminated forms to be 20 per cent, 57 per cent and 63 per cent respectively. In eight of his patients, the joint symptoms preceded the skin lesions by one and one-half months to five years. One of the Cabot cases in the New England Journal of Medicine [22] had mild attacks of pain in the shoulders and hands which occurred every spring and lasted about two weeks for a period of 11 years. Mallory [23] found that the joints showed marked synovitis but no evidence of rheumatoid arthritis.

The characteristic features are pain, swelling and tenderness of the joints with slight elevation of the surface temperature without redness. Joint deformities usually late and involving the smaller joints of the extremities have been reported by Tremaine [20] and Friedberg et al.[19]

However, Mallory [23] says "it is quite unusual in lupus to see permanent changes in the involved joints." The signs and symptoms do not seem to respond to the usual therapeutic measures.

The pathological studies of the joints reported have been meager. Tremaine [20] reported a case in which there was hypertrophy of the synovial villi, subperiosteal bone formation and inflammation with perivascular infiltration of inflammatory cells of the subsynovial and capsular tissues. Two cases reported by Friedberg et al.[19] had similar articular and extra-articular swelling associated with endothelial hyperplasia and cellular inflammation which contained giant cells and a few gram-positive cocci. The larger joints are usually affected. Ginzler and Fox [11] found only slight hyperplasia of the synovial lining cells in sections from the synovial tissues and articular cartilages of the right knee.

Fever: The fever is prolonged and remittent. During the acute phase of the disease it is usually sustained and often high. The pulse rate is proportionate to the temperature and has no particular significance.

Associated with the fever is malaise, profound prostration, sweats usually out of proportion to the demonstrable findings, and weight loss. According to Keil [24] systemic lupus erythematosus is usually free from involvement of subcutaneous tissue in any definite manner and the rapid weight loss encountered is probably the result of numerous factors.

Blood: The blood usually shows evidence of a depression of the bone marrow function, leukopenia, thrombopenia and a moderate anemia. The cause of the depression in the bone marrow is not definitely known. It may

be due to a toxic damage or to vascular lesions in the marrow. Leukopenia is often cited as a principal feature of the blood picture; however, Bauer [25] states that only 30 per cent of the 65 cases at the Massachusetts General Hospital had low leukocyte counts. Except in the event of superimposed infection or complication, one does not find a leukocytosis. Rose and Pillsbury [10] claim there is a roughly uniform reduction in the number of all the leukocyte forms, with perhaps some tendency toward a relative increase in neutrophiles.

The sedimentation rate is most often increased and remains so during clinical remissions.

Various chemical analyses of the blood show no significant changes except for an increased urea nitrogen in cases in which there is azotemia.

It is not uncommon to get false positive tests for syphilis. Davis and Ayman [26] believe the positive Wassermann test is due to a disturbed colloid and lipoid balance of the blood serum. Coburn and Pauli [27] observed in two classical cases that the factor responsible for the anticomplementary reaction was in the globulin fraction which was increased in the serum.

Serous Membranes: Inflammation of the serous membrane of the pleural, pericardial, and peritoneal cavities is of common occurrence. The involvement usually manifests itself by pain, friction rubs, and signs of effusion. All 17 patients reported by Reifenstein et al.[14] showed some evidence of pleuritis. Most of the friction rubs are recorded as pericardial. It is common for signs of pulmonary involvement to be present for many months. According to Klemperer et al.[28] the involvement of the serous membranes is from the beginning a relatively deep process by virtue of primary injury to the connective tissue.

Cardiovascular System: The pathological changes in the heart are not constant. Keil [24] finds there is gross evidence of pathologic changes in the endocardium, both valvular and mural, in approximately 30 to 50 per cent of cases. As a rule, patients with acute lupus erythematosus disseminatus die from complications other than myocardial failure. Clinically the myocardium is usually spared. The most common alteration of the electrocardiogram is low voltage in all leads which is interpreted as damage to the cardiac musculature. Contratto and Levine [29] report a case which had a distinct delay in the A–V conduction throughout the course of the disease. No digitalis was given. They go on to say that this finding in the early course of the disease, before the rash appeared, led them to consider rheumatic fever as the first probable diagnosis.

Gross,[30] in a pathological study of the hearts in a series of 23 cases, found hematoxylin-stained granular bodies especially frequently in the valves and valve pockets. He thinks "the milder, spongy, superficial valvular lesions containing degenerating, ghost-like mononuclear cells are probably earlier stages of the hematoxylin-stained bodies and almost characteristic." According to him these hematoxylin-stained granular bodies have been encountered only in systemic lupus. Klemperer et al.[28] say that these changes described by

Gross are but a part of a complex injury whose essential feature is the degeneration of the noncellular components of the collagenous tissues.

Occasionally the atypical verrucous endocarditis of Libman and Sacks [2] is found. Since their report of four cases in 1924, Gross [31] in 1932 found among 6,000 autopsies, 37 possible cases of Libman-Sacks endocarditis, of 11 of which he was certain; Baehr et al.[4] found 13 cases in their reported series of 23 cases; and in 1940 Gross [30] observed eight cases in a series of 23 cases of acute lupus erythematosus disseminatus. According to Gross [30] the primary and fundamental change in atypical verrucous endocarditis (Libman-Sacks) appears to be in the endothelium. The findings of Klemperer et al.[28] are opposed to this statement of Gross. They say that widespread damage is evident in all layers of the heart by virtue of a basic injury primarily localized in the connective tissues. Aschoff bodies and Bracht-Wachter lesions are absent from the myocardium in the atypical verrucous endocarditis.

Klemperer et al.[28] say it is the connective tissue, primarily, which is injured in acute lupus erythematosus disseminatus. The fibrinoid degeneration of collagen fibers in the adventitia produces the vascular lesions which are a mere local expression of the fundamental connective tissue injury. In contrast to other systemic vascular diseases, such as periarteritis nodosa and malignant sclerosis, the blood pressure usually remains normal. The minute vessels (capillaries) are more commonly involved in acute lupus erythematosus disseminatus.

Renal: Renal involvement is common. Mallory [22, 23] says that nephritis, even though the changes may be minimal, can be found in 70 per cent of the cases. He speaks of the nephritis as being the focal glomerular type in which one may find occasional glomerular tufts or even the single loops of the tufts like those of glomerulonephritis but with many entirely normal glomeruli. Stickney and Keith [32] describe the lesions in more detail. In their series of 15 cases, they found a proliferation of the endothelial cells of the glomerular capillaries with hyaline thickening of these capillary walls and an irregularity and thickening of the basement membrane. They regard these changes as somewhat similar to those found in acute glomerulonephritis and the toxemias of pregnancy. The lesions are considered secondary to the toxic processes and do not represent primary renal disease. Keith [33] summarizes the renal changes as follows: "(1) Renal insufficiency does not play an important rôle causing death, since severe chronic uremia very seldom occurs. (2) The histologic changes in the kidney are almost never as extensive as those seen in cases of progressive glomerulonephritis of similar duration. . . . (3) The usual renal lesions, particularly those of the glomerulus, may resemble the lesions found during the first two weeks of acute glomerulonephritis. But in lupus erythematosus renal anomalies such as albuminuria, cylindruria, and microscopic hematuria may persist for two or three years in contrast to a few weeks in the former condition and yet similar histologic findings be present. This fact suggests that the renal lesion in

lupus erythematosus is a mild reaction to a toxic agent with minimal scar formation. (4) Further study has indicated that this renal lesion is nonspecific and can be produced in various toxic conditions as, for example, lupus erythematosus, ulcerative colitis and peritonitis. (5) Finally, we have observed in some of these cases albuminuria varying periodically from grades 1 to 4 and at necropsy only minor histologic changes in the glomerulus. Such findings suggest that the renal lesion may be temporarily reversible and analogous to what sometimes occurs in the skin lesions."

The "wire-loop" appearance, due to a peculiar hyaline thickening of the walls of the glomerular capillaries, was first described by Baehr, Klemperer and Schifrin,[4] and according to the authors, it does not contain amyloid or lipoid material. Klemperer et al.[28] by using the Mallory connective tissue stain, feel that the "wire-loops" indicate a fibrinoid degeneration and collagenization of the basement membrane. This "wire-loop" appearance is not a constant finding. Mallory [34, 35] was able to find it in only one-half of the cases at the Massachusetts General Hospital. It is interesting to note that Baehr et al.,[4] in speaking about the wire loop appearance, said, "this very characteristic lesion has not been seen by us in any other human diseases, except perhaps eclampsia." It resembles the glomerular and vascular lesions described by Wadsworth [36] in horses which have been immunized by repeated intravenous injections of live bacteria, especially of the pneumococcus and streptococcus group. Klemperer et al.[28] claim to be able to distinguish the "wire-loops" in lupus erythematosus from those occurring in eclampsia, renal amyloidosis, and malignant nephrosclerosis. However, they state that the morphologic aspects of fully developed vascular necrosis obtaining in accelerated arteriosclerosis and in lupus erythematosus are indistinguishable.

Hypertension is relatively uncommon according to Baehr and his associates,[4] whereas Rose and Pillsbury [10] found hypertension present in approximately one-third of their cases.

Miscellaneous: (*a*) *Eyes:* Intra-ocular lesions are common and assume no definite pattern. Maumenee [37] points out that clinically and pathologically the white fluffy exudates do not differ from those of hypertensive retinitis. Both exudates are made up of cytoid bodies. Histologically, he found that the small superficial retinal hemorrhages were neither related to the larger retinal vessels nor to the white spots but were located in the nerve-fiber layer of the retina. The lesions are not necessarily associated with renal disease because the blood pressure is usually normal, nor are they related to bacterial embolic phenomena because the blood cultures are for the most part sterile. The evidence points to the lesions being local in origin and representing but one of the manifestations of a systemic disease. Keil [24] claims that papilledema is more common than is generally suspected. He attributes the papilledema to vascular damage, "with the transudation of edematous fluid in relation to the papilla."

Even though there may be rather extensive changes in the fundi, patients rarely complain of visual disturbances, such as blurring.

(*b*) *Central Nervous System:* The marked irritability, the clouding of the sensorium, delirium, stupor, and unconsciousness observed in some patients point to cerebral involvement. On the other hand, some patients remain mentally clear to the end. Tremaine [20] recorded the occurrence of adhesive meningitis in a single case. Keil [24] observed an instance of chronic meningoencephalitis. Jarcho,[38] in his case 5, described many of the cerebral vessels containing thrombi. Areas of distinct encephalomalacia were present in the cortex and the cornu ammonis. There were no vascular lesions in the eyegrounds. Blood cultures were sterile and even though the patient had verrucous endocarditis, there was no bacterial endocarditis. Lobar pneumonia was the terminal complication.

(*c*) *Lymph System:* Lymphadenopathy is common and it may precede the appearance of the skin lesions. Keil [24] says that the lymphadenopathy in acute lupus sometimes becomes as marked as that in tuberculosis. Goeckerman's [39] treatment of irradiation of the deep gland-bearing areas is evidently based on a belief that all the deep glands are involved. Mallory [25] speaks of a great increase in blood vessels and necrosis of the germinal centers in the lymph glands. Ginzler and Fox [11] first noted the occurrence of peculiar lesions in the lymph nodes and spleen. Microscopically the lymph nodes showed "distinctive areas of focal necrobiosis with or without peculiar hematoxylin-staining bodies"; the spleen showed "periarterial areas of necrosis of the follicular lymphoid tissue, periarterial fibrosis and intimal arterial thickening." Splenomegaly is uncommon.

Etiology: The cause of acute disseminated lupus erythematosus is still a matter of much speculation. At the present time, there are essentially three schools of thought concerning the etiology. One group, predominantly German, believe that the disease is associated with tuberculosis in most instances. A second group, mostly English, feel that it is due to a septicemia probably of the streptococcus. The third group, notably the Americans, favor the varied etiology (mostly toxic).

For a long time many authors regarded this disease syndrome as a manifestation of tuberculous infection or as an allergic response to tuberculotoxin. Goeckerman,[39] Reitmann and Zumbusch,[40] and Low, Logan and Rutherford [41] reported cases in which the lymph glands were extensively involved. Keefer and Felty,[8] in one of their cases, made an inoculum from a lymph gland which showed no histologic lesions characteristic of tuberculosis. They, then, injected the substance into the testes of a rabbit from which a human strain of tubercle bacilli was recovered. Unusual sensitiveness to tuberculin was noted by Ravogli [42] who had two patients die after the cutaneous injection of 0.001 mg. of tuberculin. Keil,[43] from an exhaustive study, concludes "that the occurrence of tuberculosis in cases of lupus erythematosus is coincidental and unrelated."

An infectious etiology is suggested by the clinical features of the disease. H. J. Templeton, commenting upon Madden's [12] paper, told of two cases of acute lupus that recovered after a vaccine, which was prepared from the

hemolytic streptococci cultured from the patients' abscessed teeth, was administered intradermally. He stated: "Whether the recovery occurred because of the vaccine or in spite of it I am not prepared to say. I believe some of the cases are streptococcal in origin, and it is possible that desensitizing therapy may be of some value." Various organisms have been recovered from the blood stream but one is inclined to think that these are terminal invaders. Blood cultures are persistently sterile in the great majority of cases. Roxburgh [44] believes "that all cases of lupus erythematosus are the result of a sensitization of the skin to light by toxins of either the tubercle bacillus or streptococcus." O'Leary [45] and Pels [46] also believe that the disorder is due to a toxemia, probably attributable to a bacterial agent. As is well known, the local Shwartzman phenomenon (intense vascular damage) occurs at the skin area previously prepared by injection of bacterial toxin if a small amount of bacterial toxin is injected intravenously 24 hours later. Apitz [47] and also Gerber [48] found that vascular lesions could be reproduced experimentally in various viscera by the repeated intravenous injection of bacterial toxin. Gerber felt that preliminary preparation in some animals with both an intradermal and intravenous injection enhanced the development of systemic vascular lesions.

Pulay [49] and Gennerich [50] were among the first to note the hypersensitiveness of patients with disseminated lupus erythematosus. Pulay thinks that the location of the skin lesions is due to photosensitivity. He attributes the photosensitiveness to any one of the products of metabolism such as glucose, acetone, hemoglobin, urea, lactic acid, hematoporphyrin and tyrosin, and other chemical substances which have been shown to produce photosensitiveness. In cases in which tuberculosis is prominent, he considered the cause to be the sensitizing action of the tuberculotoxins. Ludy and Corson [51] have recently reported the presence of hematoporphyrinuria and of lead in the skin of 15 out of 18 cases observed in Philadelphia; and they believe the disease to be increasing in frequency in this locality. Lewis [52] has pointed out that the cutaneous areas most often affected are those in which the capillaries are of the atonic type (that is, they do not respond normally to the injection of vasoconstrictor substances). Wilson [53] purposely exposed a small area of skin to ultraviolet rays; and almost immediately the patient developed a severe inflamed area that spread to the rest of the body.

Gennerich [50] believes that a sensitizing substance results from the destruction of the lymph glands by an unknown disease. The ferments of the lymphocytes are freed and circulate in the vascular system as foreign proteins which, when subjected to irritation by light, air, and mechanical agents, produce anaphylaxis. He does not think the lymphatic involvement is due to tuberculosis.

The histopathology of the disease appears to be the result of a toxic agent. Keil [54] advances the concept that acute lupus erythematosus disseminatus is a disease of unknown etiology with a vascular predilection chiefly for the capillaries and to a lesser extent, the arterioles and venules.

This would explain the wide variety and variability of visceral involvement and the protean clinical nature of the disease. However, Klemperer et al.[28] in a recent histopathological study of 20 cases of lupus erythematosus disseminatus conclude that the characteristic organic changes, previously considered as heterogeneous, can now be understood as local manifestations of the widespread damage of collagen. They go on to say that "the various concepts of lupus erythematosus as a disease with predominant localization in a single organ or as a diffuse disease of the peripheral circulation can be entertained no longer."

The rôle of the endocrines, especially the ovaries, must at least be considered as a possible contributory or predisposing factor. Certain cyclical variations in ovarian function are often associated with changes in the skin such as flushing and sometimes bleeding from the mucous membranes. Contratto and Levine [29] claim gratifying results following roentgen irradiation of the ovaries.

Therapy: Inasmuch as the etiology is not established, therapy is mostly supportive and symptomatic. Rest in bed and good nursing care are essential.

Search for and eradication of foci of infection and the use of vaccines [12] (autogenous) have their merits, but eradication of foci of infections should never be undertaken during the acute phase (Keith and Rowntree [55]).

Most of the metallic elements are contraindicated because there are commonly present leukopenia and thrombopenia. Fluids not incompatible with the renal condition are important; dextrose, administered intravenously, is sometimes an aid. Blood transfusions have given at least temporary remissions. Salicylates may be given for the fever and arthralgia.

Exposure to any form of actinic therapy is dangerous.[54] However, roentgen irradiation of the ovaries warrants a trial.[29]

Reports vary as to the effectiveness of sulfonamide therapy. So far results have not been encouraging.

Case Report

Case 1. M. E. D., aged 32, a colored housewife, was admitted September 10, 1940, and died October 24, 1940.

Complaint: "Pains in arms and legs for three weeks."

Family History: Irrelevant.

Past History: The patient had always enjoyed good health except for diphtheria, measles, mumps, varicella, and pertussis in childhood and influenza at the age of 16. She had never had any of the other infectious diseases. She had had frequent bouts of sore throats associated with trembling spells, abdominal pains and chills at the age of 12. There was no history of swollen or painful joints. Since then she had had mild exertional dyspnea. She had never had any visual or auditory disturbances prior to the present illness. There was no history of a chronic cough, hemoptysis, or night sweats. The gastrointestinal, genitourinary, menstrual and neuromuscular systems had always been normal. Her habits were exemplary and her development was normal. There had never been any skin eruption until the present illness.

Present Illness: The patient felt well until three weeks prior to admission when she was stricken suddenly with severe, constant aching pains in all her joints, but there was neither redness nor swelling. There were intermittent, sharp, aching substernal pains unrelated to meals and respirations. Associated with the arthritis were marked malaise, anorexia, headaches, vertigo, diplopia and blurring of vision; however, the latter two symptoms gradually disappeared after several days. She felt feverish and had profuse night sweats. During the weeks before admission, she suffered from chilly sensations, trembling of her limbs, nausea, vomiting, frequency and urgency of urination with incontinence, and a moderately severe cough productive of small amounts of blood streaked, rusty sputum.

Physical Examination: The temperature was 102° F., the pulse rate 80, and her respirations 32 per minute. The blood pressure was 125 mm. Hg systolic and 75 mm. diastolic. She was fairly well developed and nourished but appeared acutely ill. The patient was restless and dull mentally.

The skin was quite dry and there was evidence of recent weight loss. There was no rash, excoriation, or abnormal pigmentation. The hair was that of a normal colored female. The bases of the finger nails were slightly puffy and cyanotic.

The bones were normal. There was no tenderness or swelling.

There was no general glandular enlargement. The epitrochlears were bilaterally palpable and two or three glands were felt in each axilla.

Examination of the head revealed nothing abnormal. The optic discs were normal. The arterioles were irregularly constricted and showed A–V nicking. The venules were moderately distended. There were two small linear hemorrhages near each disc. The mouth showed some gingivitis and dental caries. The tongue was pale and there was mild papillary atrophy. The pharynx was clear and the tonsils were not enlarged.

The thorax was symmetrical and well formed. There was diminished expansion of the right lung as compared to the left. The percussion note was resonant anteriorly but there was impairment from the right mid-scapular region down. The breath sounds were clear anteriorly; they were tubular over the right base and there was also a moderate number of fine dry râles. The heart was very little enlarged to the left. The rate was moderate and the rhythm regular. The sounds were of fair quality. The pulmonic second sound was greater than the aortic. A low pitched systolic murmur was heard over the entire precordium.

The abdomen was normal. The spleen was slightly tender and palpable, just below the costal margin. The liver was not felt.

There was no acute joint swelling or tenderness; however, all joints were a little stiff. The muscles were generally tense and moderately tender. Neurological examination was negative except for bilateral sustained ankle clonus and hyperactive deep reflexes. Pelvic and rectal examinations were not done.

Laboratory Examinations:

Blood examination showed: red blood cells 4,200,000 per cu. mm.; hemoglobin 6.5 gm., 45 per cent (Sahli) (normal 14.5 gm., 100 per cent); white blood cells 4,000; sedimentation rate 60/20; volume of packed red blood cells 26. Hematocrit studies: MCV 62 cubic microns; MCH 15.4 micromicrograms; MCHC 25%. Differential count: myelocytes 0 per cent, non-segmented neutrophiles 32 per cent, segmented neutrophiles 60 per cent, eosinophiles 0 per cent, basophiles 0 per cent, lymphocytes 4 per cent, monocytes 4 per cent.

Stained smears showed marked poikilocytosis, anisocytosis, and pallor. No other abnormalities of the red cells were noted. Platelets normal. No abnormal cells. No sickling.

Eagle test was negative on three different occasions.

Blood chemistry: non-protein nitrogen 21 mg. per 100 c.c. on admission to 92 mg. per 100 c.c. three days before death. Total protein 7.3 gm. per cent. A/G ratio

2.6/4.7. Chlorides 290 mg. per cent. NaCl 478 mg. per cent. Cholesterol 130 mg. per cent. Calcium 9.7 mg. per cent. Phosphorus 5.3 mg. per cent. Phosphatase 6.0 Bodansky units. Uric acid 3.2 mg. per cent. Creatine 1.9 mg. per cent. Icterus index 5. Van den Bergh 0.2 mg. per cent, indirect reaction. Formol gel 4+.

Blood cultures were repeatedly negative. Blood agglutination, tularemia—0, typhoid H—0, typhoid 0—0, paratyphoid A—0, paratyphoid B—0, proteus X 19—0.

Urine was cloudy, yellow. Specific gravity 1.019, reaction acid. Albumin 2+. Sugar 0. White blood cells 3–4 per high power field. Red blood cells 0. Occasional granular and rare hyaline cast. Bilirubin, negative to trace. Urobilin 4+ to 0. Stool negative. No pathogenic organisms. Sputum examination showed no tubercle bacilli, 72 hour concentrations. Sputum culture showed mixed flora, no organisms predominating.

Spinal fluid was clear; 2 cells/cu. mm. one lymphocyte and one crenated red cell. Pressure normal. Wassermann reaction negative. Pandy negative. Culture showed no growth. Pleural fluid was clear, yellow. Specific gravity 1.020. Cells 510 per cu. mm., mostly lymphocytes, rare polymorphonuclear. Cultures, aerobically and anaerobically were negative. Concentration test for tubercle bacilli was negative. Guinea pig inoculation revealed no tubercle bacilli.

Tuberculin skin tests negative to 1:100 (old tuberculin).

Roentgenogram of chest (9/11/40): Outlines of right side of heart not made out. Left side seems enlarged. Aorta widened. Diffuse denseness over right lower half of lung due to consolidation or fluid. (9/20/40): Changes in both lower lung fields, due to fluid. (10/10/40): Some clearing of right lung field.

Course: On admission the patient had signs of consolidation in the lower right lung and, although the pneumococci present in the sputum could not be typed, she was started on routine therapy of sulfapyridine. Supportive therapy which included intravenous glucose and saline was also given; and on the seventh and ninth hospital days she received transfusions of 450 c.c. of whole blood. The temperature remained elevated from 101° F. to 104° F., and was septic in character. Inasmuch as some observers considered the possibility of a lung abscess the patient was given 0.45 gm. neoarsphenamine on the seventh day and every other day thereafter for a total of six doses. Sulfapyridine was discontinued on the tenth day.

Signs of fluid in the right chest became evident on the nineteenth and again on the thirty-first hospital days. Thoracentesis yielded respectively 700 c.c., and 350 c.c. of clear, straw colored fluid which was bacteriologically negative. The pulmonary consolidation in the right lung persisted and since tuberculin tests of 1:100 on the twenty-fourth day were negative the patient was started on routine sulfathiazole therapy on the thirty-second day in an attempt to combat the septic course.

About the time sulfathiazole therapy was instituted the patient developed a macular rash on the bridge of her nose which extended in a butterfly shape to both cheeks. In two days the rash became exfoliative and spread rapidly to the neck, arms, thorax and limbs. The epithelium of the involved areas desquamated in great sheets. The diagnosis of acute lupus erythematosus disseminatus was then evident. Sulfathiazole was continued for nine days, but it did not alter the rapid, downward course. The patient lost weight very rapidly and became markedly emaciated. The temperature rose very suddenly to 104° F. on the forty-fifth hospital day and she died.

Throughout her hospitalization she had a fine to coarse tremor, muscle tenderness, and moderate stiffness of the joints. The ankle clonus observed on admission gradually disappeared after three weeks. The ophthalmological appearance of the fundi remained unchanged until the dermatitis appeared and then an increasing number of small hemorrhages and exudates appeared in the fundi.

No pleural or pericardial friction rubs were ever heard. The systolic murmur present on admission was not audible several weeks later.

Patient developed an azotemia (non-protein nitrogen 92 mg. per 100 c.c.) several days before death. There was no rise in blood pressure, and examination of the urine revealed no changes other than those previously found.

*Autopsy Findings.** *Anatomical Diagnosis:* Disseminated lupus erythematosus; necroses and scarring in lymph nodes; focal necroses and hemorrhages in spleen with perivascular scars; focal necroses in pancreas; organizing fibrinous pleurisy; hyaline thickening of alveolar walls in lung; focal myocarditis, slight scarring in heart; chronic epicarditis; chronic mural endocarditis with areas of fibrinoid degeneration; healing focal necroses and periportal infiltration in liver; generalized lesions of small arteries; acute splenic tumor; organizing thrombi in ovarian veins and perivesical plexus; subacute nephritis. Purulent bronchitis (slight); unidentified fungus in a small bronchus. Calcified tuberculous focus in lower lobe of right lung; calcified peribronchial nodes; calcified tubercle in spleen. Decubitus ulcer.

Gross Findings. The autopsy was performed six hours after death. The body was that of a slender, fairly well developed, colored female. The skin of the entire body showed fine desquamation. Over the abdomen and left thigh the desquamation was more marked and there was a moderately thickened layer of cornified epithelium. A decubitus ulcer, 4 cm. in diameter, was present over the sacrum. The cervical, axillary and inguinal nodes were palpable but only moderately enlarged.

Serous Cavities: The pericardial cavity contained 60 c.c. of yellowish, slightly cloudy fluid. The pericardial surfaces were smooth but more opaque than usual. There were a few filmy adhesions over both lungs; there was no fluid. Except for thread-like adhesions over the dorsal surface of the liver, the peritoneal cavity showed nothing remarkable.

Heart: The heart weighed 350 grams. It was not dilated. The measurements of the valve rings were within normal limits. The epicardium was more opaque than usual, indicating slight thickening. The surface was smooth. No gross lesions were seen in the myocardium or endocardium. All of the heart valves were grossly normal except the non-coronary cusp of the aortic valve where several tiny spines, apparently fibrous, were attached to the corpus Arantii. The coronary orifices were normal and the vessels not sclerotic.

Lungs: The anterior surfaces of both lungs showed diffuse thickening of the pleura and a similar change was seen on the posterior surface of the right lung. Most of the thickening was due to fibrous tissue but in places there was slight roughening due to fibrin. Patchy areas in the posterior part of each lung appeared edematous. The larger bronchi contained sticky mucus. There was no gross consolidation. There was a calcified focus, 3 mm. in diameter, in the middle of the right lower lobe. The lymph nodes at the hilum of each lung contained calcified foci.

Spleen: The spleen weighed 170 grams. There were scattered little fibrous tags attached to the capsule. The splenic pulp had a somewhat rusty coloration. The splenic vein and artery were patent, as well as the portal vein.

Liver: The liver weighed 1560 grams. On section it appeared paler than usual; the lobulation was moderately accentuated. The gall-bladder and bile ducts were grossly normal.

Kidneys: The right kidney weighed 240 grams and the left 150 grams. The capsule of each kidney was not adherent. The external surface of the kidney was smooth. Both kidneys appeared pale and swollen. On section the cortical striae were straight but somewhat blurred. The lining of the renal pelves and ureters appeared normal. About each ureter the connective tissue was thicker than usual, including the tissue about the ovarian veins as well. Both ovarian veins contained thrombi. The thrombus material was mainly decolorized and in places hyaline. In the region of the broad ligament on the left the thrombus material was red and apparently fresher.

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Bladder: The bladder was contracted and its lining normal.

Pelvic Organs: The uterus was small. There were a few myomata a few millimeters in diameter. A cyst, 2 cm. in diameter, containing old blood, was present in the left ovary. The tubes were grossly normal. Around the neck of the bladder there were thrombi in small veins.

Lymph Nodes: The peritracheal nodes were moderately enlarged. Some of them contained well walled-off old caseous foci and a few such lesions were calcified. The lymph nodes around the abdominal aorta and iliac vessels were larger and soft. These on section showed a bulging, somewhat nodular, cut surface. There were a number of little granules visible which suggested follicles, and about some of these there were narrow hemorrhagic zones. Other lymph nodes were firm and rubbery in consistency and on section appeared white and fibrous. The peri-pancreatic lymph nodes and those at the hilum of the liver were moderately enlarged.

The pancreas, adrenals, stomach and intestines were grossly normal. The neck organs showed nothing remarkable. The tonsils were not obtained with the specimen. The femur bone-marrow was moderately hyperplastic. The thyroid and parathyroids showed no gross lesions. There was very little subcutaneous fat. The muscle in the thigh showed nothing. The record contained no mention of the joints which apparently were not examined.

Brain: The meninges over the surface of the brain were grossly normal. The vessels at the base were not sclerotic. The dorsal anterior convolutions were distinctly smaller with wider sulci, indicating much more atrophy than one would expect at this age.

On sectioning the brain the ventricles were not enlarged. Throughout the brain, particularly in the white matter, there were minute reddish streaks (this may have been merely pigment from the embalming fluid). In the corpus striatum, particularly the thalamus, there were a number of tiny holes, in the gross like minute cysts. These were probably minute areas of perivascular atrophy.

The hypophysis and pineal showed nothing abnormal.

Microscopic Findings. Heart: There were minute fibrous scars in the myocardium. There were loose accumulations of fibrous tissue about fairly numerous small vessels. These were concentric and completely surrounded the vessel. In a few places there were early suggestively granulomatous lesions with mononuclear cells. Occasionally a perivascular lesion extended into the surrounding myocardium and the proliferative fibrous lesion included very shrunken atrophied muscle fibers. Minute blood vessels showed a pink-staining material in their walls, sometimes with perivascular mononuclear cells and proliferation of the intimal layer. Others showed largely necrosis.

In the endocardium there were flat little patches of fibrous scar tissue. In some of these there were minute areas, or central-longitudinal streaks, of hyaline necrosis. The diffuse opacity of the epicardium, as seen in the gross specimen, was due to a thickening of the fibrous tissue forming loose bundles of collagenous material. Not infrequently there were little patches of necrosis with a few mononuclear cells. Occasionally one encountered a red-staining, wavy or spiral appearing, coagulation of connective tissue perpendicular to the surface of the heart—"fibrinoid degeneration." There was diffuse but slight infiltration with lymphoid and mononuclear cells.

Lungs: There was an organizing fibrinous pleurisy with very little cellular infiltration. There were a few polymorphonuclear leukocytes and a few mononuclear cells. Beneath the exudate the pleural connective tissue formed a thin hyaline layer staining deeply with eosin. No bacteria could be demonstrated in the pleural exudate.

In the parenchyma of the lung there was no fresh pneumonia. There were areas of collapsed lung tissue in which mononuclear cells were found in the collapsed air spaces and also in the alveolar walls. In these areas there was a hyaline thickening

of the alveolar walls. Many of these little streaks contained an occasional mononuclear cell, suggesting that a former exudate was in process of being incorporated into the alveolar wall. Where the lung was more expanded these hyaline thickenings of the alveolar walls could still be found in numbers and had an appearance very like that of the so-called "wire-loop" lesions described in the kidney in this condition. In part the bronchi were contracted and contained only a little mucus with a few cells. In the same sections other bronchi were normally wide. Only here and there did a bronchus contain a purulent exudate. Stains for bacteria showed a few Gram positive cocci, some of them in polymorphonuclear leukocytes. In one section two minute bronchi contained a purulent exudate and hyphae of a fungus. The mycelium was wide and short and in the hematoxylin and eosin sections seemed to show septa. Other preparations from the same block failed to show this organism, and smears from many bronchi from the gross lung were spread and stained without showing any other of these organisms.

The vessels in the lung not infrequently were the seat of a hyaline necrosis but in only one vessel was anything suggesting a thrombus to be found.

The changes in the alveolar walls of the lungs were not unlike the "wire-loop" lesions described in the kidney and to our knowledge have not been previously mentioned.

Spleen: There was an acute splenic tumor characterized by clumps of cells in the splenic pulp, often about tiny vessels and with the character of plasma cells or cells with lymphocytic nuclei and a basophilic cytoplasm. There were multiple hemorrhages and minute necroses in the splenic pulp. Occasionally there were concentric hemorrhages about Malpighian bodies. In some instances these showed coagulated blood and organization. There were some perivascular scars and others in intermediate stages suggesting that they were the result of the organization of the hemorrhages mentioned. Many little vessels in the Malpighian bodies were hyaline. There was swelling and hyalinization of the fibrous tissue in the capsule. Multiple minute areas of necrosis with a few polymorphonuclear leukocytes could be found, suggesting that this was the early stage of the process.

Pancreas: The pancreas was well preserved. There were minute areas of necrosis with early scarring. In one such area which was a little larger, there were large swollen collagenous fibers about a small artery and nerve. In the periphery of the pancreas there was a small focus of "fibrinoid degeneration" in the peripancreatic fat, and extending along one of the fibrous septa. In this latter area there were a few mononuclear cells.

Liver: The capsule was not thickened. There were a few small scars extending into the liver beneath the capsule and in these early scars there were swollen and bright red staining collagenous fibers. The periportal spaces showed early scarring with diffusely scattered lymphocytes and less frequent mononuclear cells. In the parenchyma the liver was moderately but diffusely fatty. The lipoid change was mainly periportal but so widespread as to be seemingly midzonal. There were focal lesions in which the liver cells themselves were necrotic. In other tiny lesions the parenchymal cells were gone and mononuclear cells formed a small nodule, suggesting healing focal necroses.

Adrenal: The tissue was well preserved since the cells of the medulla showed good fixation. In the zona glomerulosa the cells were shrunken and the capillaries dilated. Many of the shrunken atrophied cells appeared necrotic. There was a diffuse thickening of the capsule, in large part fibrous with areas of "fibrinoid degeneration." There were fibrous collars about small and medium sized blood vessels.

Kidneys: There was an acute and subacute nephritis and most of the glomeruli showed swelling of the tuft epithelium and interstitial tissue with compression of the capillaries. There were coarse granular precipitates of protein material in some

of the glomerular spaces. Only an occasional glomerulus showed a thin layer of adhesions between the glomerulus and capsule. Here and there were hyaline necroses, usually in the portion of the glomerulus near the entering arteriole. In these instances in which the arteriole was present, some showed early hyaline changes. Here and there were older glomerular lesions with the character of an intercapillary glomerulonephritis. Ring-like thickenings were also present like those of the "wire-loop" lesions, but these were hardly distinguished from the more general interstitial alteration and seemed to be simply a later part of the same process. The small and larger arteries showed little. About some of the small arteries there were adventitial cellular accumulations of plasma and mononuclear cells.

The tubular changes were more pronounced than the glomerular lesions. In general the tubules were dilated, with low epithelium. There were numerous casts. Loops of tubules everywhere were the seat of hyaline droplet degeneration. Not infrequently in such areas the tubule contained laked red blood cells. In other areas where the cytoplasm was filled with these coarse granules the cells were actually necrotic and there was early regeneration. Here and there shrunken groups of tubules contained deep red staining small casts and in the interstitial tissue there were lymphocytes and plasma cells and a suggestion of very early scarring.

In those sections which showed the renal pelvis, the interstitial epithelium was normal except for slight autolytic changes and there was no pyelitis.

Bladder: The bladder appeared contracted. Despite the contraction and natural thickening of the submucosa, it still seemed fibrous and scarred. There was no evidence of a chronic cystitis. In the bladder wall a small artery had a hyaline necrosis of its intimal layer with fragmentation of cells and a slight inflammatory reaction.

Uterus: There was atrophy of the uterine mucosa and there were multiple minute hemorrhages. The lower layer had a number of glands, whereas in the superficial half of the uterine lining there were only a few tubular glands approaching the surface. In the uterine wall the vessels were greatly thickened. The intima in such cases showed a hyaline thickening and also an obliterative endarteritis which was more like that found in the uterus in a person of 60 to 80 years than in one 32 years of age. These vessels showed thick hyaline layers in the intima. In other vessels the intima was fibrous and many of the small arteries showed an intact intimal and medial layer with a broad zone of hyaline change about them. Even the uterine muscle appeared atrophied, and there was a diffuse hyalinization.

Ovaries: There was a hemorrhagic cyst in one ovary with early organization of the blood clot. In the margin there were no definite lutein or follicular cells which were recognizable. Nearby there was a smaller cyst with a fibrous organizing layer in the periphery and a great deal of hemosiderin pigment. In this same section there was a well developed follicle in an intermediate stage of maturation.

Ovarian vessels: The sections across the ovarian vessels containing thrombi showed veins containing thrombi in all states of organization. The vessel walls showed proliferative changes but no definite alterations that could be considered the result of inflammation. Many small arteries had very thick hyaline bands in the position of the internal elastic lamella overlaid by a proliferative change in the intima. Some of these vessels showed an infiltration of mononuclear cells in the adventitia and media.

Fallopian Tube: There was a chronic salpingitis with adhesions between the papillary projections of the folds. In some of these there were small hemorrhages.

Pharynx: In the sections of the pharynx there was only a slight round and mononuclear cell infiltration in the submucosa. The epithelial layer was intact. In one of the sections a microscopic lesion was found in which there was a dense hyaline change in a group of collagenous fibers.

Thyroid and Aorta: The aorta itself was normal. As part of the section the pleural and subpleural tissue was present. Here there was a zone of granulation tissue with only a few polymorphonuclear leukocytes and many plasma and mononuclear cells.

Lymph Nodes: There were nine blocks from representative lymph nodes, both the peripheral and internal groups. In all the nodes the solitary follicles had practically disappeared. The lymph cords and sinuses were inconspicuous. Sometimes throughout the whole node, and in all of them in patchy fashion, there was an increased vascularity and these tiny vessels were thickened. In some places the capsule was thick and fibrous and often bands of cellular connective tissue extended into the node. About numerous small vessels there was what appeared to be new-formed cellular connective tissue around the group of vessels, and this was infiltrated with mononuclear cells. Fresh necroses were present in half the sections. These varied in size from microscopical areas to the largest which was 5 mm. in diameter. In the necrotic areas the cells and nuclei were fragmented. The larger of these lesions were not unlike the fresh suggestively caseous lesions of tularemia. In one node the lesion extended to the periphery where the capsule was involved in an inflammatory lesion. Here there were accumulations of polymorphonuclear leukocytes, mainly mononuclear cells, and in small areas the capsular tissue was necrotic. There was inflammation in the fat about the node. Distended lymphatics contained leukocytes. Small vessels, both lymphatics and arteries, showed an interstitial and perivascular inflammatory lesion. The cells present here were plasma and mononuclear cells.

Several of the nodes showed considerable hemosiderin pigment in phagocytic cells. No tubercle bacilli nor bacteria could be demonstrated in the necrotic lesions.

Skin: Five blocks were prepared from representative portions of the skin lesions. Microscopically all showed similar changes. There was a very thin layer of epithelial cells. The keratinized layer on the surface was not particularly conspicuous, but scaling bits of keratinized epithelium could be found. The papillae of epithelium were small and simplified. There was a good deal of melanin pigment both in the basilar layer of the skin and in the connective tissue just beneath. The subepithelial layer of connective tissue was thicker than usual and lacked its usual loose structure. The fibers were swollen and formed a much more compact network than usual. The deeper layer of coarse collagenous fibers showed nothing unusual. There was practically no inflammatory reaction with the exception of a ring, one to two cells deep, around minute vessels. Some of these little vessels were thickened.

The sweat glands in the sections were normal except for an occasional hyaline thickening of the basement membrane, and in a very few cases a few lymphocytic cells about an isolated acinus.

Bone-marrow: The femur bone-marrow was largely fatty, and there was a considerable degree of the gelatinous change commonly seen in emaciated states. The islands of blood-forming tissue were few and widely scattered.

Brain: In the sections of brain the meninges were normal. There was moderate cortical atrophy with widening of the perivascular spaces. In the pons there were perivascular hemorrhages but no lesions of the vessels themselves. In the basal nuclei there were spaces about the vessels which could well be the minute cyst-like lesions described in the gross. In the lenticular nucleus numerous small vessels had rings of intramural and perivascular granular calcification, a lesion which is not infrequently encountered in all sorts of cases. In this section there was one small area of rather old encephalomalacia.

Eye: A hemorrhage in the retina near the nerve head was present in a section from one eye. In this same section a small vessel external to the sclera was thickened and hyaline. No other lesions were found.

Hypophysis and Pineal: No lesions were found.

Anatomical Comment. In view of the rapid progress of the disease process in this case and the resulting short duration, the autopsy findings present features of great interest. Both early and older lesions are present and, with the exception of a verrucous endocarditis, practically all that have been observed in this condition. The absence of any severe or widespread terminal infection makes it possible to be reasonably certain that practically all the changes observed are part of the disease acute lupus erythematosus disseminatus itself. The slight bronchitis and the small decubitus ulcer were all the infected lesions observed, and death was caused in all probability by nephritis and uremia.

The necroses and inflammatory lesions in the lymph nodes, which in general receive less attention in descriptions of this condition, remind one of the lesions of typhoid fever or tularemia. In this case some of the necrotizing lesions did not involve the whole of the lymph node structure in the area, and it seems plausible that the healing of such lesions would result in the scarred vascularized nodes or portions of a node here found side by side. One is also intrigued by the possibility that the perivascular hemorrhages and necroses in the spleen in their healing and resolution leave as an end result the perivascular fibrous thickenings which are so common in lupus. The necrotic lesions involving lymph nodes, spleen, pancreas and blood vessels with the variety of tissues involved, make it difficult to subscribe to the thesis that the lesions of lupus indicate primarily a disease of collagenous tissue. The focal hepatic necroses of this case could heal without leaving a recognizable scar and the focal myocardial and pancreatic lesions in the end would appear as nondescript scars.

The peculiar thickenings of the alveolar walls in the lungs in this case suggest the incorporation of an organized exudate into the alveolar wall rather than an interstitial change in the wall itself. A similar but much more localized lesion of this sort can not so infrequently be found in the lungs of persons usually with emphysema and chronic bronchitis and patchy pneumonia, in whom all stages in the organization of an intra-alveolar exudate and the apparent fibrous thickening of the alveolar wall can be observed. Probably these eventually practically disappear.

In a disease which so regularly shows some degree of damage to the kidney clinically and definite lesions at autopsy, the active nephritis shown in this instance is not surprising. The "wire loop" lesions, although present here, are not so conspicuous as pictured in other cases, and in any event are obscured by the more general changes. It seems reasonable to assume that they are the result of former minimal lesions.

The autopsy findings furnish no clue to the etiology of the disease, but the picture as a whole as it is present in this case would suggest some as yet undiscovered infectious agent.

Case Reports

Case 2. M. C., aged 38, a white housewife, was admitted February 25, 1938, and died March 5, 1938.

Complaint: "Skin rash for one month."

Family History: Father had eczema and one sister had "skin trouble" for 10 years, presumably eczema.

Past History: The patient's general health had been fairly good. She had had varicella, measles, mumps, pertussis, and diphtheria in childhood without apparent sequelae. She denied other infectious diseases. In November 1933 she was seen in the Psychiatric Clinic of the University of Maryland Hospital, and it was the impression of those who saw her that she was "intellectually and emotionally weak" and that "her reaction type was that of a poorly organized hysteria." Therefore, little credence could be placed in some of her answers. She was subject each winter to frequent head-colds which were accompanied by very little malaise, fever, and sore throats. The visual and auditory senses had been normal prior to her present illness. In 1932 she had all of her teeth extracted because of "extreme decay and abscesses." She denied a chronic cough, hemoptysis, night sweats, and pain in the chest. She had had exertional dyspnea and palpitation for a number of years, but no ankle edema, or nocturnal paroxysms. Her gastrointestinal system had been essentially normal except for chronic constipation and occasional bleeding attributed to hemorrhoids. Urinary function had always been adequate and symptom-free. The catamenia had been normal up to 1936 when she began to have some menorrhagia and metrorrhagia and a feeling of heaviness and numbness in her pelvis. A supravaginal hysterectomy was done at the West Baltimore General Hospital because of uterine fibromata and endometrial hyperplasia. She had had three normal pregnancies previous to 1936. The neuromuscular system was significant only in the fact that she had always "fainted" at the slightest provocation. Her habits were excellent. She had had no skin rash prior to the present illness.

Present Illness: The onset of the patient's present illness actually occurred in March 1937 when, for the first time, she noticed a "red spot" on the center of her forehead. The lesion was approximately 4 cm. in size and got no larger. There was no history of the lesion scaling, oozing, itching, or burning. However, one month later she became more concerned about it, presumably for cosmetic reasons. She consulted her family physician who told her the lesion was "ring worm" and gave her some salve to apply. Soon thereafter similar lesions appeared on the cheeks, nose, and right side of the forehead. She then consulted another physician who advised her to spend most of the time in the sunshine. She followed his advice and the lesions spread to the neck and shoulders; at the same time her hair began to fall out in great quantities. As she was obviously getting worse she returned to the physician several months later (during the summer) and he gave her five or six "light treatments" which caused the lesions to spread further over the face, neck, and shoulders and to burn and itch. The treatments were discontinued and the patient was placed on a special diet free from meats and eggs, and all fruits except bananas. She remained on this diet until admission. She got along fairly well during the rest of the summer and fall except for general malaise, nervousness, and weakness. Her skin lesions cleared only slightly, but the alopecia became so marked by January that she went to the University of Maryland Hospital Skin Clinic. The diagnosis of lupus erythematosus was made and she received a course of Bismuth Salicylate 0.2 gm. each week for five weeks. The day following the last injection (February 2, 1938) there was a marked exacerbation of her skin lesions which became "fiery" red and began to spread to the arms and chest. Two days later the entire body was involved. The skin became slightly edematous. There was some oozing and much

scaling. There was marked malaise, weakness, and fever. She stated that during the two months before admission she had lost at least 20 pounds.

Physical Examination: The temperature was 102.2° F., the pulse was 100, the respirations were 20, and the blood pressure 100 mm. Hg systolic and 40 mm. diastolic. The patient was an undernourished and poorly developed woman whose age was difficult to approximate by inspection. She was mentally alert and coöperative.

The entire skin of the body was covered with confluent, erythematous, vesicular, scaling lesions. The skin was warm, tender and it blanched with pressure. The scaling was most marked on the head, neck, arms, hands, and thorax. The lower portion of the legs was covered with loose skin under which there appeared to be a small amount of serum. The feet were covered with large papules interspersed with apparently normal skin. There was almost complete alopecia and the remaining hair was very fine in texture.

The bones were normal. There was no tenderness or swelling.

The cervical and epitrochlear glands were not felt. There were a few, medium-sized, discrete, non-tender glands in the axillae. The inguinal glands were also discrete and slightly enlarged.

There was excessive lacrimation of the eyes. The lid margins were reddened. The pupils and extraocular movements were normal. The fundi showed many small areas of whitish exudate with several larger ones above and below the left disc. There was no apparent papilledema. The skin lesions extended into the auditory canals but the drums were normal. The mouth revealed complete adentia and an ulcer on the lower left anterior portion of the gum. The pharynx was not injected. The tonsils were normal in appearance.

The thorax was not remarkable. The breasts were small, underdeveloped and contained no masses or tenderness. The lungs were resonant throughout. No abnormal sounds were heard. There were no râles. The heart was not enlarged to the left or right. The rate was moderately fast, the rhythm was regular. The sounds were of good quality. A soft systolic murmur was audible over the entire precordium.

The abdomen was scaphoid. A midline scar extended from the umbilicus to the symphysis pubis. The liver and spleen were not felt. There was no fluid, abnormal masses, or tenderness.

There was no joint tenderness or swelling. Neurological examination was normal except for hyperactive reflexes and absent abdominal reflexes.

Pelvic examination revealed a small normal cervix. The fundus and adnexae were not felt. There were no masses or tenderness. Rectal examination was normal.

Laboratory Examinations: Blood examination showed: red blood cells 3,500,000 per cu. mm.; hemoglobin 72 per cent (Sahli) (normal 14.5 gm. 100 per cent); white blood cells 1,000 to 3,850.

Differential Count:

	2-26-38	3-3-38
Myelocytes	7%	0%
Non-Segmented neutrophiles	20%	11%
Segmented neutrophiles	43%	37%
Eosinophiles	1%	9%
Basophiles	0%	0%
Lymphocytes	27%	40%
Monocytes	2%	3%

Stained smears showed no abnormality of the red blood cells except pallor. The platelets were normal. No parasites seen. Eagle (blood serology) test negative.

Blood chemistry: Non-protein nitrogen 29 mg. per 100 c.c.; sugar 118 mg. per 100 c.c.; total protein 6.1 gm. per cent; A/G ratio 3.7/2.4; chlorides 265 mg. per cent; NaCl 437 mg. per cent; cholesterol 110 mg. per cent; calcium 7.8 mg. per cent; phos-

phorus 3.1 mg. per cent; icterus index 3; Van den Bergh 0.1 mg. per cent (indirect reaction).

Blood cultures: (3–2–38) *Staphylococcus albus* (hemolytic), 100 colonies per c.c. (3–3–38) *Staphylococcus albus* (hemolytic). Cultures presumably contaminated by the skin which could not be prepared adequately.

Urine cloudy, yellow. Specific gravity 1.020; reaction acid; albumin, 0—2+. Sugar 0. Occasional white blood cell. Occasional red blood cell. Casts —0. Stool negative.

Pleural fluid (3–4–38) clear, straw colored, 300 c.c. Cells: 25 polymorphonuclears. Culture negative. Protein 11 gm. per cent. (3–5–38) 250 c.c. grossly bloody fluid. Culture negative.

Roentgenogram of chest (portable) (3–3–38) showed dense clouding at the right base, probably due to fluid.

Course: The patient was given a high caloric and high vitamin diet supplemented with cevitamic acid and vitamin B. The skin was treated with olive oil and later with calamine liniment and carron oil. The lesions improved markedly; there was more scaling and evidence of progressive epithelization with healing.

The temperature on admission rose from 102.2° F. to 103.4° F., and remained elevated and septic in character until the sixth hospital day when it leveled off and remained about 100° F. until death three days later. Salicylates started on the fourth hospital day had no effect.

On the seventh hospital day she suddenly became dyspneic and examination revealed signs of fluid at the right base. A thoracentesis yielded 300 c.c. of clear fluid. There was improvement in her dyspnea. She was given a second transfusion (550 c.c.) and developed a mild reaction. However, signs of cardiac insufficiency became evident and she was rapidly digitalized. A thoracentesis done on the ninth hospital day yielded 250 c.c. of bloody fluid. That afternoon the patient died without much change in her condition.

Case 3. C. L., aged 33, a colored housewife, was admitted August 8, 1940, and discharged October 7, 1940.

Complaint: Multiple joint pains for three months.

Family History: Mother died in a mental sanatorium. One sister died in a tuberculosis sanatorium.

Past History: The patient had always enjoyed good health until the present illness. She had had only the usual childhood diseases without sequelae. She had been subject to frequent sore throats until 1932 when her tonsils and adenoids were removed. There was no history of other infectious diseases. There were no visual and auditory signs or symptoms. She denied a chronic cough, sputum, night sweats, and hemoptysis. The cardiac, gastrointestinal, urinary and neuromuscular systems were negative. Her catamenia was normal. Following a miscarriage in 1925 she had had a tubo-ovarian abscess. A right salpingo-oöphorectomy, excision of corpus luteum cyst of the left ovary, and an appendectomy were performed at the University of Maryland Hospital. She had had no skin lesions prior to her present illness.

Present Illness: The patient was well until May 1940 when she developed slight pain and stiffness in her fingers. About the same time she noticed stiffness in the anterior portion of the thighs, especially when walking up and down stairs. The stiffness in the hands disappeared within two weeks but that in the thighs persisted. It seemed to be worse in the mornings, but quickly improved after arising. There was no history of chills or fever. She continued to take one white tablet before meals and one green tablet after meals until admission without apparent relief.

Approximately one month later she noticed minimal pigmentation and roughness of the skin over the bridge of the nose and the point of the chin. The lesions dis-

appeared from the face within two weeks but similar lesions appeared on the left breast, in the left axilla and on the left shoulder.

She experienced marked malaise, anorexia and weight loss of approximately 30 pounds.

Physical Examination: The temperature was 100° F., the pulse rate 110, and the respirations 20 per minute. The blood pressure was 105 mm. Hg systolic and 70 mm. diastolic. The patient was a fairly well developed and nourished colored woman who appeared her stated age and who was in no obvious discomfort.

The skin was warm and rather dry. There was an area of slightly increased pigmentation over the bridge of the nose. On the chin there was an area of increased pigmentation with several papules about 2 mm. in diameter. An area two to three inches in diameter was present on the left breast. This lesion was dry, scaling and had increased pigmentation. There were similar lesions at the insertion of the left deltoid muscle and along the left posterior axillary line.

The bones were normal except for suggestive fusiform swelling of the phalanges. All joints were supple and free from pain.

There was no local or general glandular enlargement.

The eyes were perfectly normal to external examination. The fundi showed rather large (½ — 1 D.D.) dull, white areas which were unlike exudates usually seen in arteriolar disease. They were not fluffy and were generally situated between an artery and vein; however, occasionally a vessel was partially covered. Most of the exudates were within 2 disc diameters of the disc. A few hemorrhages were present. No Rothe spots were seen. The discs and vessels appeared normal. The ears, nose, mouth, and pharynx showed no abnormalities.

The breasts were not tender and contained no abnormal masses.

The thorax was well formed and symmetrical. Expansion was equal and adequate. The lungs were perfectly clear to percussion and auscultation. The heart was slightly enlarged to the left and right. The sounds were of good quality. There was a soft systolic murmur heard over the entire precordium. The rate was moderately fast and the rhythm was regular. No friction sounds were audible.

The abdomen was scaphoid. A midline incision scar extended from the umbilicus to the symphysis pubis. The liver edge extended just below the costal margin. The spleen was not palpable. No abnormal masses or tenderness were elicited.

Pelvic examination was normal except for absent right adnexa. No ulceration of mucosa. Rectal examination was negative and confirmed the pelvic examination.

Neurological examination was perfectly normal.

Laboratory Examinations:

Blood examination showed: red blood cells 2,630,000 per cu. mm.; hemoglobin 8.5 gm., 52 per cent (Sahli) (normal 14.5 gm., 100 per cent); white blood cells 2,480; sedimentation rate 68/20; volume packed red blood cells 22.

Hematocrit studies: MCV 85 c.μ. MCH 32 micromicrograms, MCHC 33%.

Differential Count:

	8/8/40	8/23/40
Myelocytes	4%	0%
Non-segmented neutrophiles	1%	7%
Segmented neutrophiles	75%	77%
Eosinophiles	0%	1%
Basophiles	0%	0%
Lymphocytes	17%	12%
Monocytes	3%	3%

Stained smears showed moderate anisocytosis and poikilocytosis. There were no polychromatophilia, stippling, or nucleated red blood cells. No parasites were seen. No sickling. Fragility test normal. Reticulocytes 1.0 per cent. Platelets 1,300,000,

normal appearance. Bleeding time 45 seconds. Clotting time 2 minutes 15 seconds. Clot retraction 1 hour 30 minutes. Sternal puncture normal. Eagle test negative.

Blood chemistry: nonprotein nitrogen 24 mg. per 100 c.c. (8/8/40). Total protein 7 gm. per cent (8/28/40); 4.7 gm. per cent (9/20/40). A/G ration 2.6/4.6 gm. per cent (8/28/40); 2.3/2.4 gm. per cent (9/20/40). Cholesterol 240 mg. per cent. Uric acid 4.8 mg. per cent. Icterus index 5. Formol gel 4+. Blood culture negative. Blood agglutination for *B. abortus,* Melitensis, suis, 0.

Urine cloudy yellow. Specific gravity 1.006, 1.018, 1.014, pH acid. Albumin 2+, 0. Sugar 0. White blood cells 3–8 per high power field. Occasional red blood cell and granular cast. Culture: *B. subtilis.* Fishberg concentration test (8/12/40), specific gravity 1.010 (1 hr.), 1.008 (2 hrs.), 1.010 (3 hrs.). Phenolsulphonphthalein excretion: (15 min.) 0, (1 hr.) 20, (30 min.) 25, (2 hrs.) 0, total 45 per cent. Stool negative. Basal metabolic rate —1.

Biopsy of skin showed some edema of subcutaneous connective tissue and slight evidence of chronic inflammation. No specific lesions. Excision of cervical lymph gland—normal. Electrocardiogram showed normal mechanism. Roentgenogram of chest, heart and aorta normal. Lungs clear. Hips and pelvis—nothing abnormal seen.

Course: The patient was placed on the regular hospital diet and bed rest. Her complaints were never acute. The skin lesions remained unchanged. A biopsy of the skin showed some edema of the subcutaneous tissue and slight evidence of chronic inflammation but no specific lesions. The arthralgia gradually disappeared without specific therapy. Soon after admission she rapidly developed ideas of reference and persecution which grew progressively worse. Finally on August 20, 1942 she prevailed upon her husband to take her home against the will of the attending physicians. Two days later she was admitted to the psychiatric division in a mental state of confusion and partial disorientation with hallucinations and suicidal attempts. Her course on the psychiatric wards was uneventful and short. Dr. Esther Richards thought the patient had a delirium, and it was the impression of the house staff that the delirium was dependent upon toxic factors probably associated with the lupus. Dr. A. E. Maumenee of the Wilmer Institute at Johns Hopkins Hospital saw the patient, and he said that perhaps the same pathological process occurred in the brain as in the eye grounds; that is, a swelling of the neuroglia fibers. It is of significance to note that the mental state cleared up as the exudates in the fundi became fewer in number, smaller and more grayish. The patient was transferred September 17, 1940 to the medical service for further study. Physical examination was the same except for slight general glandular enlargement. The left cervical glands later became prominent and slightly tender. One of these lymph nodes was removed for biopsy but it showed no abnormality. As the glandular enlargement progressed the skin lesion of the nose became puffy and dusky red and spread to the malar eminences back to ears and to the forehead. The line of demarcation was sharp. The lesions elsewhere on the body showed little change. A few fresh hemorrhages appeared in each fundus, but there was no increase in number or size of the exudates.

The temperature was only moderately elevated and ranged from 99° F. to 100.5° F. The blood picture remained essentially unchanged. There was a persistent albuminuria. The patient continuously asked to go home and inasmuch as she was getting no worse it was decided to let her go home on October 7, 1940. One month later the patient died from a fairly acute illness without hospitalization.

Case 4. D. R., aged 18, a white girl, was admitted June 24, 1940, and died February 18, 1941.

Complaint: Pain and swelling of the joints of six months' duration.

Family History: Father and mother died at 59 years of asthma (probably cardiac) and "neuritis."

Past History: The patient had had only the usual childhood diseases which were uncomplicated. At the age of 12 she had an "attack of rheumatism" about which she remembered little except that she was placed at bed rest for three months under a doctor's care. She knew of no complications that might have occurred at that time and stated that no restrictions were placed on her activity following this attack. She was advised to have her tonsils and adenoids removed but this advice was rejected. She had never had any visual or auditory symptoms. There was no history of chronic cough, hemoptysis, or night sweats. The gastrointestinal, genitourinary, menstrual, and neuromuscular systems had always been normal. Her development was normal and her habits were excellent. There had never been any skin eruption until the present illness.

Present Illness: At Christmas time, 1939, the patient had a sore throat and began to suffer with fleeting pains in her joints with redness and swelling. At this time, too, she noticed for the first time a "scabby" skin eruption about her eyes that progressed to include her cheeks as well. She did not seek medical aid but treated herself by alcohol rubs and short periods of rest when incapacitated. During the next six months, the joint pains separately and fleetingly involved the knees, ankles, feet, shoulders, elbows, wrists, and hands. The skin eruption cleared somewhat on the face but spread to involve the lower arms and legs. The day prior to admission she had an acute flare-up of her joint manifestations which were so severe that she was unable to get relief.

Physical Examination: The temperature was 100° F., the pulse rate 90, and respirations 26 per minute. The blood pressure was 134 mm. Hg systolic and 84 mm. diastolic. She was a well developed and nourished red-haired white female who appeared her stated age. She lay in bed in rather acute distress and was obviously unwilling to move.

The skin was hot and dry, and generally clear except for comedones and the following lesions. At the outer canthus of each eye and in a very imperfect "butterfly" area over the bridge of the nose and upon the cheeks were red, scaly, dry, maculopapular areas with indefinite borders. Similar larger patches appeared upon the extensor surfaces of the forearms and lower half of the upper arms and lower anterior surfaces of the legs.

The bones were normal. There was no tenderness or swelling of the bones.

There was no general glandular enlargement.

Examination showed the head to be perfectly normal. There was no alopecia or lesions of the scalp. The eyes were completely negative except for very moderate tortuosity of the retinal arteries. The ears and nose were normal. The mouth was negative except for dirty, carious teeth. The pharynx revealed small uninflamed tonsils. There were many enlarged lymph nodes in the anterior cervical triangles.

The thorax was symmetrical and well formed. The breasts were normal and virginal. The lungs were perfectly clear to percussion and auscultation. The heart was full sized, globular, but otherwise negative. No murmurs were heard.

The abdomen was normal except for slight tenderness to deep palpation over the left kidney region. The liver and spleen were not felt.

Pelvic organs were those of a normal virginal female.

The extremities revealed the skin lesions as described above. There were swelling, tenderness and pain on motion at both wrists and the left elbow. There was some local heat but no redness. The left foot was arched acutely and fixed. The neurological examination was normal except for generalized hyperactivity of the deep reflexes.

Laboratory Examinations:

Blood examination showed: red blood cells 4,270,000 per cu. mm. Hemoglobin 12.5 gm., 88 per cent (Sahli) (normal 14.5 gm., 100 per cent). White blood cells

6,150. Sedimentation rate 32 mm. (corrected). Volume of packed red blood cells 40 c.c. Hematocrit studies: MCV 93 c.μ, MCH 29 micromicrograms, MCHC 31%. Differential count: myelocytes 0 per cent, polymorphonuclears 74 per cent, eosinophiles 0 per cent, basophiles 0 per cent, lymphocytes 23 per cent, monocytes 3 per cent. Stained smears appeared normal. No abnormal cells seen. No parasites. Wassermann reaction negative. Kline screen test doubtful.

Blood chemistry: nonprotein nitrogen 28 mg. per 100 c.c. Sugar 87 mg. per 100 c.c.

Urine, yellow. Specific gravity 1.020, pH acid. Albumin 0. Sugar 0. White blood cells 0. Red blood cells 0. Casts 0. Phenolsulphonphthalein 25 per cent in one hour.

Kidney function tests were unsatisfactory because of patient's inability to cooperate, but all specimens ranged between 1.003 and 1.020 in specific gravity. A heavy trace of porphyrin was found in the urine by chemical analysis.

Stool negative. Electrocardiogram showed normal tracings in Leads I, II, and III, and notching of T in Lead IV. Teleroentgenogram revealed a globular heart and clear lung fields without evidence of pericardial or pleural change. The joints showed no changes from normal.

Course: The patient was placed on salicylates with dramatic relief of her joint symptoms but no effect on the erythema. When salicylates were discontinued without the patient's knowledge, the joint pains returned and the salicylates had to be started again. During her stay in the hospital, the patient's appearance was so suggestive of acute lupus erythematosus disseminatus that investigations were carried out along this line. Ultraviolet ray sensitivity was tested over the skin of the abdomen showing a marked erythema without vesiculation after exposure for 10 seconds and moderate erythema after as short a time as five seconds. A skin biopsy from one of the areas of erythema produced by ultraviolet ray showed changes consistent with chronic inflammation including perivascular round cell infiltration. All skin lesions gradually disappeared. Biweekly sedimentation rate determinations remained consistently between 32 and 36 mm. corrected. She continued to have slight (to 99.2° F.) fever. After 60 days of bed rest, a tonsillectomy and adenoidectomy were performed under general anesthesia. Recovery was uneventful. Feeling that nothing further could be done for the patient, and that a gain of five pounds in weight was a sign of satisfactory progress, she was discharged on August 17, 1940 as improved with instructions to follow a rest régime at home and to report back for observation.

She was subsequently seen on September 7, 1940 (one month after discharge) at which time she had no complaints. The urine was negative and the sedimentation rate was 32 mm. (corrected). She was again seen November 14, 1940 (three months after discharge) at which time her urine was still negative. Red blood cells 3.63; hemoglobin 57 per cent; white blood cells 6,700; polymorphonuclears 74 per cent; lymphocytes 19 per cent; eosinophiles 3 per cent; monocytes 4 per cent; sedimentation rate 27 mm. (corrected); volume index 98; mean corpuscular volume 85.1 cμ.

Five weeks prior to her second hospital admission February 17, 1941, the patient was forced to remain constantly in bed, largely because of weakness. During this time she had several attacks of pain in her left flank. She said she had seen several small red spots over her body and arms. There had been no hemoptysis. On the date of admission, she had substernal pain and while on her way to the bathroom, she "fainted" and because of this was brought to the hospital.

Physical Examination: The temperature was 100.2° F., the pulse rate 128, and the respirations 42 per minute. The blood pressure was 110 mm. Hg systolic and 72 mm. diastolic. She showed evidence of weight loss and was obviously critically ill. She was extremely dyspneic and orthopneic. Respirations were rapid and shallow.

The skin was very pale, and there were no petechiae or eruptions of any kind. Mucous membranes were also pale but were otherwise negative, except for two pe-

techial hemorrhages in the right lower conjunctival sac. Ophthalmoscopic examination was negative. There was slight engorgement of the neck veins. The cervical glands were not enlarged.

The lungs were clear except for occasional moist râles at both bases. Examination of the heart showed a double apical impulse. There was a systolic thrill at the apex. The heart was moderately enlarged to the left. The sounds were of poor quality. At the left border of the sternum, there was a protodiastolic gallop. There was a soft systolic murmur at the apex and some observers noted a low-pitched mid-diastolic rumble just inside the apex. Pulses were equal at the two wrists. Examination of the abdomen was unsatisfactory because the patient could not lie down owing to the marked dyspnea and orthopnea. The liver was probably two fingers' breadth below the costal margin. The spleen was not felt. The inguinal glands were small and rubbery.

There was no edema of the extremities. Slight cyanosis was perceptible in the nail beds.

Laboratory Examinations:

Blood examination showed: red blood cells 3,280,000 per cu.mm. Hemoglobin 8 gm., 58 per cent (Sahli) (normal 14.5 gm., 100 per cent). White blood cells 19,850. Differential count: myelocytes 0 per cent, non-segmented neutrophiles 2.5 per cent, segmented neutrophiles 88 per cent, eosinophiles 1 per cent, basophiles 0 per cent, lymphocytes 7.5 per cent, monocytes 1 per cent. Stained smears showed moderate anisocytosis and poikilocytosis of the red blood cells with central achromia. Platelets were abundant. Blood culture was negative.

Course: The patient was given digitalis and morphine, but she became rapidly worse and died 14 hours after admission. Permission for an autopsy could not be obtained.

Comment

These four cases were selected primarily because they illustrate some of the variable clinical manifestations of acute lupus erythematosus disseminatus.

The skin lesions in case 1 did not appear until almost two months after the onset of the present illness which was characterized by polyarthritis, marked malaise, anorexia, fever, night sweats, and signs of nephritis. Two weeks after hospitalization the patient was tested with old tuberculin 0.1 c.c. in dilutions of 1 : 1,000,000; 1 : 100,000; 1 : 10,000; 1 : 2,000; and 1 : 100 over a period of 10 days. It is interesting to note that the skin lesions appeared six days after the last tuberculin injection (0.1 c.c. of 1 : 100) which was negative after 48 hours. Whether or not the tuberculin precipitated the dermatitis is not certain but it is a possibility. Concomitant with the appearance of the skin lesions was the presence of an increasing number of small hemorrhages and exudates in the fundi. Pleural effusion occurred on two occasions, but it was not a prominent feature of the clinical course. The patient developed azotemia (nonprotein nitrogen—92 mg. per 100 c.c.) several days before death. There was no rise in blood pressure or additional urinary changes.

The onset of the present illness in case 2 was marked by the skin eruption. Even though the dermatitis was typical it was not recognized, and the patient was advised by her physician to take sun baths. The danger from ultraviolet exposure is clearly illustrated by the increase in severity of the skin

lesions and the general condition. This case also illustrates the deleterious effect of a heavy metal. She received a course of bismuth salicylate 0.2 gm. intramuscularly each week for five weeks. The day following the last injection, there was a marked exacerbation of her skin lesions which became "fiery" red and began to spread to the arms and chest. Two days later, the entire body was involved. Pleural effusion was a terminal event.

It is of significance to note in case 3 that the delirium cleared up as the exudates in the fundi became fewer in number, smaller, and more grayish. One seems justified in postulating that the same process existed in the brain and eyes; namely, a swelling of the neuroglia fibers. Unfortunately, an autopsy could not be obtained. Arthralgia and myalgia preceded the skin lesion by one month; and fresh hemorrhages appeared in the fundi during an exacerbation of the skin lesion, just as occurred in case 1.

The arthralgia and skin lesions occurred simultaneously in case 4. The response of the polyarthritis to salicylates was excellent and when the salicylates were discontinued without the patient's knowledge, the joint pains returned. The electrocardiogram was normal. Even though there was dramatic relief of her joint symptoms with salicylates and there was a history of "an attack of rheumatism" five years previously, the skin lesions were so suggestive of acute disseminated lupus erythematosus that the following investigations were carried out. Ultraviolet ray sensitivity was tested over the skin of the abdomen and showed a marked erythema without vesiculation after exposure for 10 seconds and moderate erythema after as short a time as five seconds. A skin biopsy from one of the areas of erythema produced by ultraviolet ray showed changes consistent with chronic inflammation including perivascular round cell infiltration. The skin lesions gradually disappeared without any specific therapy and they did not recur even during the terminal stages. The appearance of renal damage and anemia occurred very late during the course of her illness. The cardiac murmurs which were heard, for the first time, during her last hospital admission could be explained on the basis of the severe anemia. However, they suggest the possibility of a verrucous endocarditis.

All four of the cases had skin lesions, prolonged fever, leukopenia with secondary anemia, nephritis, and a remittent cachectic course. Cases 1, 3, and 4 had polyarthritis and arthralgia. Cases 1 and 2 had pleural effusions. Case 4 may have had verrucous endocarditis. The duration of the disease in this group of patients ranged from two months to 12 months, the average being approximately eight months.

Summary

A review of the literature on acute lupus erythematosus disseminatus is presented. An attempt is made to emphasize the clinical aspects. Four cases, two colored and two white females, are used to illustrate the variability of the symptom-complex.

Acute lupus erythematosus disseminatus is a disease of unknown etiology associated with widespread visceral lesions predominantly involving the kidneys, lymph nodes, blood vessels, serous and endocardial surfaces, as well as the skin. There is a marked predilection for females in the second and third decades. The prognosis is grave and the average duration of the disease is approximately 18 months. The clinical picture is variable; however, the skin lesions, leukopenia with secondary anemia, arthritis, prolonged fever, and signs of renal involvement are prominent features that should make the diagnosis possible. The avoidance of any form of actinic therapy, except perhaps the roentgen irradiation of the ovaries, and the danger of eradication of foci of infection during the acute phase cannot be overemphasized.

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RELATION OF EMOTIONS TO INJURY AND DISEASE: A CALL FOR FORENSIC PSYCHOSOMATIC MEDICINE*

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I. Introduction and Historical Review

Few problems of scientific proof have been so perplexing to court and counsel, and to the expert witness, as those which arise in the "nervous shock" cases. A, intentionally or negligently, presents a psychic stimulus to B, with or without impact,§ and B alleges that in consequence he suffered "nervous shock" or some disabling injury or disease for which he should be allowed to hold A in damages. How far shall the law go in recompensing B for the alleged effects of fright or other emotions so induced, and how shall the courts deal with the problem of proof? These two questions are somewhat interrelated. We do not propose to make the instant paper a catalogue of legal cases, but to use legal doctrine as a mere background to enable us to project problems of proof and to suggest certain criteria for testing claims of causation.

Rights of recovery for invasions of personality, whether caused by direct trauma or by psychic mediation, are to be determined by the law of torts.[1] One cannot do justice to the legal doctrine of the "nervous shock" cases un-

* Received for publication August 7, 1943.

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§ We prefer to think of "impact" as indicating any force brought to bear on another's body or sensory apparatus, whatever the medium for transmission of the stimulus. If this concept were adopted, it would be simultaneously recognized that all cases of "nervous shock" involve impact, by visual, auditory or other sensory bombardment. But since the historical legal connotation of "impact" has been restricted to cases where a material object or person is brought into bodily contact with another individual, we use impact in this sense in mentioning court cases.

[1] A "tort" is a wrongful invasion of some right of personality or of property of another, causing injury in respect to which the law will give redress by money damages without proof of any contractual or consensual relations between the actor and the person acted on. Tort law might be characterized as the sum total of those legal prohibitions whereby the sphere of individual existence is protected from negligent, intended or malicious conduct of strangers. "The law of torts" is thus a generic term covering a wide variety of such wrongs, including "assault," "battery," "trespass," "conversion" (wrongful appropriation of another's personal property), "false imprisonment," "malicious prosecution" for a crime not committed, "slander and libel," "negligence," "fraud or deceit," "breach of trust," a stranger's act in "inducing breach of contract," "malpractice" of a professional man, violation of patents, trade-marks, copyrights or other vested property rights, "unfair competition" in business and other such proscribed conduct. It is through this branch of the law that such individual rights have received greatest legal protection and the citizen has been insured against unnecessary risks of injury in a crowded society.

less he keeps sharply in focus the limit of protection which the common law [2] has given to interests of personality.

(1) There is legal authority to the effect that if A, without producing any impact, *willfully* or *maliciously* causes B to suffer mental anguish, B may be allowed to recover damages without proving that any physical injury or actual disability was caused thereby.

Example: Plaintiff was a widow who supported her two minor children by the wages she earned. These wages were exempt by law from attachment and the defendant collection agency knew this fact. For the purpose of causing her mental anxiety and thus coercing her into paying a $28.75 coal bill due to one of its customers, defendant wrote a series of threatening letters. No physical violence was threatened, but plaintiff was told that a direct appeal would be made to her employer, with the assurance that this would be successful and "we will bother him until he is so disgusted with you that he will throw you out the back door." And again: "You will settle in full your account with the above through this office within the next five days or we will tie you up tighter than a drum." Defendant also intimated that plaintiff was as bad as a criminal.

Plaintiff suffered no physical injury or disability, but sued defendant for malicious invasion of mental tranquillity, alleging that the course of conduct indulged by defendant caused her mental pain, anguish and humiliation. The jury so found and returned a verdict in her favor, and from judgment entered thereon, defendant appealed to the Supreme Court of Iowa, contending that plaintiff had not proved any legal grounds for recovery of damages. That court described the legal problem presented thus: "We therefore have our problem reduced to the proposition as to whether or not recovery may be had in a case where the act is willful, as distinguished from negligent, and where there was no physical injury and no assault, and where the plaintiff in the action did not suffer from fright, but from mental pain and anguish caused by the willful act of the defendants."

Held, affirming judgment: P is entitled to recover; the willful quality of the conduct takes it out of the class of mere negligence. The Iowa Supreme Court said: "The rule seems to be well established where the act is willful or malicious, as distinguished from being merely negligent, that recovery may be had for mental pain, though no physical injury results. In such a case the door to recovery should be opened but narrowly and with due caution."

Barnett v. Collection Service, 214 Iowa 1303, 242 N.W. 25 (1932).

(Note carefully that Iowa is one of the states which refuses to permit recovery of damages for injuries due to fright without impact if the psychic stimulus is caused by the mere *negligence* of defendant. Lee v. City of Burlington, 113 Iowa 356, 85 N.W. 618 (1901).)

(2) If A, without producing any impact, *willfully* or *maliciously* does an act calculated to cause B mental anguish or nervous shock, B may recover damages for any physical injury actually caused thereby. The injury being more substantial and certain, grounds for allowing recovery here are even stronger than in (1) supra.

Example a: Plaintiff was returning home along a dark road in company with her husband when they noticed they were being pursued by another car. It had been

[2] The "common law" or judge-made law, consisting of the decisions and supporting opinions of the appeal courts on problems of law brought up from the trial courts, constitutes a precedent for disposing of like cases in the future, if there be no directly controlling provision of a constitution or statute.

noised about that one B, a notorious murderer, was at large in the community. In fact the pursuing car was operated by deputy sheriffs, and in their anger at plaintiff's failure to stop her machine, they fired 12 shots, one of which buried itself in the back of the front seat. Plaintiff was so prostrated by fright and nervous shock that she was confined to hospital for 13 days and to bed for six or seven weeks. She sued the deputy sheriffs and recovered a verdict and judgment from which the defendants appealed.

Held, by Michigan Supreme Court: Judgment affirmed.

Firing of the shots was an intentional act constituting an "assault" (intentionally putting another in reasonable apprehension of immediate bodily harm), and plaintiff may recover for the nervous shock even though there was no actual impact.

(Note, carefully, that Michigan is one of the states which refuses to permit recovery of damages for injuries due to fright without impact if the psychic stimulus is caused by the mere *negligence* of defendant. Nelson v. Crawford, 122 Mich. 466, 81 N.W. 335 (1899).)

Example b: Plaintiff M was a maid in the house of Y, whom a Miss X was then visiting. X claimed to have certain letters from a Major Z, among them items which Z believed to have been forged. Z desired to inspect the letters to see if they were genuine, and to that end hired defendant, D_1, a retired Scotland Yard man, now operating as a private detective, to obtain them. D_1 sent his agent D_2 to the house of X with instructions to bribe the maid if necessary. Instead, D_2 attempted to gain access to the letters by threatening M. At an interview on July 16, 1917, in X's house, D_2 told M that he was a detective inspector from Scotland Yard representing the military authorities, and that she was the woman they wanted as she had been corresponding with a German spy. In fact M was engaged to a German named Neumann, who since July, 1915, had been interned in the Isle of Man, and she had been corresponding with him against the wishes of her relatives. According to M's testimony, the threat caused her great fright and a nervous shock which expressed itself in immediate symptoms and led on to neurasthenia. There was medical testimony that such a stimulus could cause the nervous disability of which M complained, and in an action against D_1 and D_2 M got a verdict and judgment against both, for £250.

Held, on appeal, affirmed.

Janvier v. Sweeney (Court of Appeal, England), 2 King's Bench (1919) 316.

Even though the injury is not intended or desired by the actor, he nevertheless is liable in damages for actually causing it if the wrongful act which he intentionally does is one calculated to produce nervous shock. This is the rationale of Janvier v. Sweeney, supra, and of example c.

Example c: In Wilkinson v. Downton (Queen's Bench Division, Eng. 1897), 2 Q.B. 57, defendant, as a practical joke, falsely represented to plaintiff that he had been sent by her husband to say that he had been smashed up in an accident and was lying in hospital E with both legs broken, and that she was to come for him at once in a cab. The effect on plaintiff was to produce nervous shock with immediate vomiting and subsequent disability lasting for several weeks. P sued D. The appeal court upheld a verdict in P's favor for more than 100£. It stressed the fact that the stimulus was of a nature likely to upset a person of normal constitution, and took pains to say: "These consequences were not in any way the result of previous ill-health or weakness of constitution; nor was there any evidence of predisposition to nervous shock or any other idiosyncrasy."

(3) Most courts hold that if A *negligently* causes B to suffer mental anguish or transient fright, with no resulting disability or injury, B cannot

recover damages. The law does not protect B against transient invasions of his mental tranquillity caused by mere negligence of another.

Example a: X and his wife, Y, sued D, a contractor, for negligently blasting on a railroad right of way so that stones were thrown upon the roof of plaintiff's nearby house, causing them to suffer fear and mental anxiety for the personal safety of themselves and their child. Plaintiffs, suing on a negligence theory, recovered verdict and judgment for $264 in the trial court.

Held, on appeal: Judgment reversed: No damages can be recovered for fright, there being no other injury.

Wyman v. Leavitt (Maine Sup. Ct.), 71 Me. 227 (1880).

Example b: Defendant railway company negligently frightened plaintiff's horses, causing them to break his wagon and put him in fear of his own personal safety. Plaintiff did not allege or prove any physical injury, but obtained a jury verdict and a judgment for damages based on "great mental suffering, vexation and anxiety of mind" caused thereby.

Held, on appeal, in answer to certified questions: Judgment reversed. There can be no recovery of damages for momentary fright or mental anguish caused by negligence of another, unaccompanied or followed by actual injury. Gulf, Colorado and Santa Fe Railways Co. v. Trott (Tex. Sup. Ct.), 86 Tex. 412, 25 S.W. 419 (1894).

(Note that Texas is one of the states which permits recovery if *injury* or *disability* is produced by fright, negligently caused, even though there was no contemporaneous physical impact. Gulf, etc. Railroad Co. v. Hayter, 93 Tex. 239, 54 S.W. 944 (1900).)

(4) If A negligently effects physical contact with B, the law allows B to tack on claims for mental pain and anguish caused thereby, including fright, and thus allows compensation for mental disturbance by way of what has been called "parasitic damages" when no primary recovery could be had for the latter standing alone.[3]

Example: This is well illustrated by the celebrated case of Spade v. Lynn and Boston Railroad, 168 Mass. 285, 47 N.E. 88 (1897). Plaintiff, a hypersensitive young woman, homeward bound to Chelsea on defendant's subway train, was jostled when an inebriated strap hanger was put off the car by the conductor, and she allegedly suffered such fright from the transaction that nervous shock caused her to be ill for some time thereafter. On the first trial no capital was made of the trivial impact with the inebriated man, and the Supreme Judicial Court treated the case as one of mere fright without impact and denied recovery for the alleged physical injury. Judgment for plaintiff was reversed and the case was remanded for a new trial.

On the second trial, plaintiff profited by this judicial lecture and alleged and proved that "The defendant conductor in removing a drunken man from the car jostled another drunken man who was standing in front of the plaintiff, and threw him upon her." Plaintiff again recovered a verdict and judgment in the trial court. The Supreme Judicial Court treated this contact with plaintiff's body, caused by defendant, as a battery (unconsented, intended touching of another), for which the law would allow some recovery, and held that damages for "nervous shock" due to fright could be tacked on to the primary cause of action. Justice Holmes said: "By something of an anomaly, consequences of the defendant's conduct which would not

[3] For instance, the intentional conduct may be such as to give the injured person a primary cause of action for assault, battery, trespass, malicious prosecution, defamation, wrongful arrest, seduction or some other tort. In all these cases the courts allow the plaintiff compensation for mental anguish as a parasitic element of damages.

of themselves constitute a cause of action may at times enhance the damages, if the conduct has some other consequence for which an action lies." (Here, a battery.)

Spade v. Lynn & Boston Railroad, 172 Mass. 488, 52 N.E. 747 (1899). (Judgment reversed on other grounds.)

In the "nervous shock" cases we are confronted with a preliminary question of public policy, namely: To what extent shall the law protect interests of personality of the idiosyncratic or excessively vulnerable person against injury from stimuli created by an actor in prosecution of his legitimate affairs?

With these important points of legal principle in mind, we may turn to a historical survey of the "nervous shock" litigation to discover more about the nature of the problems that arise and the adequacy of the judicial response.

A. Recovery of damages for "nervous shock" in English law.

It is an interesting fact that no plaintiff had the audacity to make a claim in England for injury from fright or other emotional stimulus allegedly caused by negligence of another until very late in the nineteenth century. Perhaps this was due to the unwillingness of medical men, in light of then existing knowledge, to appear as expert witnesses and postulate a probable connection between stimulus and disability. However, we know from various allusions in medical literature that medical science for many centuries had entertained certain ill-defined beliefs that emotional upset of sufficient intensity might produce injurious bodily consequences. The more likely explanation for the late appearance of these cases in courts of law is that English barristers were aware that the common law of England afforded very incomplete protection against invasions of mental tranquillity. It had been settled law in England for some time that there could be no recovery for fright or other disturbance of mental tranquillity caused by mere negligence of a defendant. Indeed, this seems to be the law today not only in England but in the United States, with possibly a few unimportant exceptions.

We must remember also in connection with this problem that the concept of "nervous shock" had not crystallized to any degree during the past century, and the legal mind would naturally tend to consider nervous shock as a mere species of invasion of mental tranquillity, and so to regard it as not actionable. Which of these considerations was most responsible for late arrival of "nervous shock" cases in court must remain speculative, but the fact is that the first English case, decided in 1888, did not arise in England at all, but in Canada, and reached England on appeal to the Privy Council which then was the court of last resort for reviewing decisions of the Dominion Courts.

In Victorian Railways Commission v. Coultas,[4] the facts were that James Coultas, with his wife Mary and relatives, on May 8, 1886, at about 9:00 in

[4] (Privy Council, Eng.) 13 App. Cas. 222; 57 L. J. P. C. 69 (1888).

the evening, was driving home in a buggy, and in so doing came to a crossing over the defendant's railway line. The defendant's gate-keeper negligently opened the near gate and admitted the buggy to the crossing when it was unsafe to do so because a fast moving train was approaching. "The gate keeper directed them to go back, but James Coultas, who was driving, shouted to him to open the opposite gate, and went on. He got the buggy across the line, so that the train, which was going at a rapid speed, passed close to the back of it and did not touch it. As the train approached Mary Coultas fainted, and fell forward in her brother's arms." Thereafter an action was filed on behalf of Mary Coultas alleging that as a result of defendant's negligence in exposing her to the peril of being killed by its train, she ". . . received a severe shock and suffered personal injuries, and still suffered from delicate health and impaired memory and eye sight." The opinion of the court does not show the symptoms of which Mary Coultas complained, nor the extent or duration of her illness, but from the evidence it is safe to say that the sole diagnosis was "nervous shock." There was some medical evidence to the effect that she received a severe nervous shock from the fright and was made ill for an indeterminate time thereafter as a result. One doctor testified that he was unable to detect any physical damage, and he put down her symptoms to "nervous shock."

On this state of facts a jury in the Canadian court found that the defendant's negligence produced the injuries complained of and awarded Mary Coultas a verdict for £400. They also returned a verdict in favor of her husband in the amount of £343 2s. for medical expenses incurred in her behalf. The defendant appealed to the Supreme Court of Victoria, and on December 14, 1886, this tribunal affirmed the judgment, holding that the damages awarded were not too remote to be recovered; that proof of "impact" was not necessary; and that the female plaintiff could recover damages for physical and mental injuries caused by the fright. The defendant took a further appeal to the Privy Council (England), which reversed the judgment for plaintiffs and ordered judgment to be entered for defendant.

In arriving at this result, the English court rested its decision upon four grounds, namely:

(1) Damages of this character are too remote, because such an injury is not an ordinary consequence;

(2) To recognize a right of recover would give rise to increased litigation;

(3) The problem of proof would be very great and a wide field would be opened for fictitious suits or imaginary claims;

(4) No precedent in English law could be found from times past authorizing such a recovery.

Some of these reasons for refusing recovery are obviously vulnerable to attack. As regards the second reason assigned, it must be clear that

courts exist for the sole purpose of giving redress in proper cases, and it is no argument against recognizing a cause of action that to do so would increase litigation. Nor is the fourth reason assigned one calculated to appeal to the intelligent man. If it were true that a right of recovery could never be recognized unless some prior case on like facts had permitted recovery, the flexibility and power of growth of the common law would be lost and no means would be open for giving legal protection to entirely new species of interests or claims which arise in the progressive evolution of the social order. This, of course, has never been the law, and both the second and fourth grounds assigned by the court for refusing recovery may be dismissed as unworthy.

On the other hand, the fears which the English court felt about the problem of proof and the difficulty of sorting out the meritorious "nervous shock" cases from unmeritorious claims, was a brilliant recognition, though perhaps somewhat intuitive, that no adequate standards existed in medicine itself for appraising such claims. Furthermore, close analysis of the Coultas opinion clearly shows that the court may have been influenced in refusing recovery by a feeling that the case involved more of an invasion of mental tranquillity than any actual physical injury due to fright. It was said by one or two English writers subsequently that Mary Coultas suffered a miscarriage as a result of her fright, but it is an important and striking fact that Privy Council opinion does not mention any such physical consequence as having been caused by the stimulus. Probably we must construe the medical evidence and the language of the court together to signify that the "nervous shock," in the court's opinion, produced merely transitory symptoms with no detectable physical injury or disease. Notice, for instance, the language which Sir Richard Couch used in the opinion rendered on behalf of the Privy Council:

> "According to the evidence of the female plaintiff her fright was caused by seeing the train approaching and thinking they were going to be killed. Damages arising from mere sudden terror unaccompanied by any actual physical injury, but occasioning a nervous or mental shock, cannot under such circumstances, their Lordships think, be considered a consequence which, in the ordinary course of things, would flow from the negligence of the gate keeper. If it were held that they can, it appears to their Lordships that it would be extending the liability for negligence much beyond what that liability has hitherto been held to be. Not only in such case as the present, but in every case where an accident caused by negligence had given a person a serious nervous shock, there might be a claim for damages on account of mental injury. The difficulty which now often exists in case of alleged physical injuries of determining whether they were caused by the negligent act would be greatly increased, and a wide field opened for imaginary claims. The learned counsel for the respondents was unable to produce any decision of the English courts in which, upon such facts as were proved in this case, damages were recovered. . . . It is remarkable that no precedent has been cited of an action similar to the present having been maintained or even instituted, and their Lordships decline to establish such a precedent. They are of opinion that the first question, whether the damages are too remote, should

have been answered in the affirmative, and on that ground, without saying that impact is necessary, that the judgment should have been for the defendants."

If the court in the Coultas case meant to imply that the evidence would warrant only a finding of transient mental disturbance negligently caused by defendant, without any resulting physical injury or disability, and that this would afford no basis for recovery, the vitriolic criticism later made of this case by law writers is unwarranted, for as we have said, such in main is still the law both in England and in the United States. It must be admitted, however, that no man exists with mind so keen that he can say with certainty what the language of the Coultas case means. For purposes of historical analysis it is enough to say that subsequent English courts and writers, when confronted by the somewhat ambiguous language of the Coultas opinion, took it to mean that the court intended to deny a plaintiff's right to recover damages even for physical injury or disease if it occurred without impact but solely as the result of a psychic stimulus negligently created by the defendant.

The English law quickly veered in the opposite direction and recognized the right of a plaintiff to recover for physical injury caused solely from psychic stimuli to which the defendant negligently exposed him, and this even though there was no physical contact or so-called "impact." While the case of Bell v. Great Northern Railway Company[5] actually was an Irish case, its influence on English law was such that one is entitled to regard it as a starting point in the new line of reasoning. The facts of this case were quite interesting. Plaintiff, Mary Bell, a 49 year old married woman, allegedly in good health theretofore, on Sunday, June 12, 1889, took passage for an excursion on defendant's train. In the course of the journey, the train was unable to negotiate a steep incline, and the crew unhooked some of the rear coaches to allow them to roll back down the hill. Plaintiff was not on this section of the train and "the portion of the train she was in went on, and then it gave a jerk and reversed towards Armagh, and went back very fast. She heard rattling of chains and heard cries of 'Jump out; jump out: you'll all be killed.' The carriage doors were locked; and she saw people jumping out through the windows. There was a steep embankment at one side; and the train was going back very fast. Witness and all the people in the carriage were frightened. The train came to a curve, and pulled up suddenly. Witness was then standing up, and was thrown down; and the people in the carriage were all thrown about. She remembered nothing more of how she got out of the carriage; and she was in Armagh till the Monday week after the accident, and then went home to Carrickfergus."

According to plaintiff's testimony, she was unable after the accident to do anything, owing to her injuries. In a trial, the jury found that defendant was negligent in so operating the train and returned a verdict in favor of plaintiff for £300 and in favor of her husband for loss of services and medical expenses for £50.

[5] (Queen's Bench and Exchequer Div.) 26 Law Reports (Ireland) 428 (1890).

In view of the fact that this case is a cause célèbre in the law of "nervous shock," it is worth while to notice the type of evidence offered to prove injury.

> "The plaintiff's daughter was examined and proved that in June, 1889, the plaintiff went on a visit to a lady in Armagh, and was up to that time in good health. The plaintiff came back about the Monday week after the accident, and witness hardly knew her; she looked as white as death, and trembled. She could not sleep at night; and when she fell asleep she awoke screaming. The plaintiff got gradually worse, and continually complained of her head and side. On the morning of July 7, 1889, at 3 o'clock, plaintiff had been in bed; and witness, who was sleeping in the next room, found her on the floor, screaming. The doctor was then called in. The plaintiff's mind was entirely deranged; and she began throwing things out of the bed. Ever since the accident plaintiff had been in bad health; previously she was the strongest woman in the house.
>
> "On cross-examination the witness deposed that the plaintiff was very nervous, and seemed as if she had got a great fright, and been shocked. She was always talking about the train, and people jumping out, and, before the last shock, about a soldier lying dead. After July she got slightly better.
>
> "The plaintiff's son-in-law deposed that he resided in Armagh; and hearing of the accident, drove out to the scene of its occurrence. He found the plaintiff lying on her side on the embankment, and she did not know him. He carried her to the car, and put her into it, and brought her to Armagh, where, on her arrival, she was put to bed. Witness did not believe she would live till the next morning. When the plaintiff recovered consciousness she talked very queer. She remained in Armagh till the Monday week following. Witness knew her for twenty years; and she was, up to the time of the accident, a strong, healthy woman.
>
> "Three medical witnesses were then examined, and deposed that the plaintiff was suffering from fright and nervous shock; and one of these witnesses deposed that her condition might result in paralysis."

The defendant appealed from the judgment in favor of plaintiff. The appeal court affirmed the judgment, refusing to follow the reasoning of the Coultas case. As a matter of fact, there was enough minimal impact in the fall itself to satisfy the requirements of those modern courts which will not allow recovery for nervous shock without impact. The court made no capital of this fact, however, nor was any claim made that the physical injuries asserted to have been caused flowed in any part from the fall to the floor. The Bell case represents a complete judicial antipathy to the reasoning of the Coultas case.

The court in the Coultas case was willing to say as a matter of law that disability as a result of mere fright was too remote in expectation to be a proper element of damages. Justice Palles in the Bell case was willing to say that the proper test was whether the disability actually produced by the emotional stimulus negligently created by the defendant was a "reasonable and natural consequence of such great fright," leaving it to the jury to pass on the question. Neither court denied the possibility that a psychic stimulus might actually cause a physical result or injury, and neither court made its decision turn upon the necessity for any impact. The courts in the two

cases really differed on the score of legal policy. The court in the Coultas case felt that such injuries were too bizarre and remote in expectation to be fairly charged up against the defendant as actor, and it was reënforced by its deep doubt about the problem of proof. The court in the Bell case, it will be noted, was willing to individualize each case by leaving it to the jury to say whether the disability or injury actually caused was a reasonable and natural consequence of the fright. This point of view is probably more just and scientific than to attempt any universal generalization about remoteness of damage, such as the Coultas case indulged. On the other hand, the court in the Bell case passed over with naive complacency the difficulties of the problem of proof, being content to assume that there was not more danger of imposition in this species of case than in any other where medical testimony might be required.

It is very important to get these patterns of thought in mind, for a great many American courts have traveled the same mental paths in deciding whether they will allow recovery of damages in cases of alleged "nervous shock" without impact. The smug confidence of the court in the Bell case about the ease of protecting the purity of proof is belied by the very facts therein involved. The medical evidence of causation, as set forth in that case, is subject to serious doubt. Mrs. Bell, it will be recalled, was able to continue her journey and it was not until three weeks after the frightening stimulus that her disability appeared, an interval too long to warrant the drawing of a causal connection between stimulus and effect. Furthermore, the case indicates that she suffered from symptoms suggestive of a preëxisting neurological or psychiatric disorder. There are allusions in the record to "before the last shock," and the like, showing that distinct shocks were suffered some time after the fright stimulus was generated and indicating that Mrs. Bell's complaints probably arose from independent cerebral vascular accidents not connected in any way with her frightening experience. It is interesting and somewhat anomalous that in the Bell decision, which is thought to have laid down a just basis for recovery in the nervous shock cases, the verdict itself in favor of plaintiff was probably unjust.

This result arises from the fact that courts of law were not then able to weigh the sufficiency of medical evidence, a situation which is largely true even today. As a crude response to this problem, the courts early adopted the view that medical testimony was to be treated like ordinary lay testimony, and if there were substantial disagreement between witnesses, the jury should be entitled to credit either version. This means that if two doctors appear in court, knowing nothing about the mechanisms of nervous shock, but willing to assert opposite conclusions in the form of expert opinions, there is no means whatever for preventing a miscarriage of justice except the hopeful but remote possibility that the lay jury in guessing might in some cases hit upon the right answer.

By a succession of cases the doctrine of the Bell case has been uniformly upheld in England both in ordinary tort actions and in workmen's compensa-

tion proceedings. In England a plaintiff may recover for actual injury or disability caused by a psychic stimulus negligently presented by a defendant actor, without any need for demonstrating so-called "impact." [6]

B. American decisions on nervous shock.

The first American cases began to come into court almost contemporaneously with the early Irish and English cases. American judges had to deal with the same plexus of problems and policy considerations which confronted the English courts. They either reacted sympathetically to the Coultas view or reached an opposite result, following the line of English cases ushered in by the Bell decision. Whatever the formulations and reasons pressed into service in recognizing or refusing a right of action for "injury without impact," one of the salient factors has been the judicial attitude toward difficulties of proof.

Many American courts have felt that a bar cannot be set up against all meritorious claims simply because imposition or fraud may sometimes creep in and shabby claims get unmerited redress. They feel that the balance of injustice is less if the court recognizes a right of action and assumes the risks inherent in the problems of proof.[7]

[6] Actually, the first case of nervous shock without impact was the unreported Irish case of Byrne v. Great Southern and Western Railway Company (1882) in which plaintiff, a telegraph operator in defendant's station, got a severe fright when a negligently set switch permitted D's locomotive to enter a siding, break down a permanent buffer and destroy one wall of the telegraph office. We have no record of the medical testimony, but plaintiff apparently suffered more than temporary disability from the fright, for he was awarded damages of 325£. On cross-examination, the plaintiff said: "A hair of my head was not touched; I swear I received no physical injury; I got a great fright and shock; I do not mean a physical shake; it was the crash and falling in of the office, and shouts of the clerks saying they were killed; I saw part of the office falling in; I believed it was all falling in."

The Court in the Coultas case evidently was unaware of this legal precedent, but Justice Palles, in the Bell case, called attention to it and mentioned the fact that he personally was the trial judge who presided over the Byrne case.

Subsequent English authorities have followed the Bell case: Dulieu v. White & Sons, 17 The Times L.R. 555, 2 K.B. 669 (1901); Hambrook v. Stokes Brothers, Ltd., 41 The Times L.R. 125 1 K.B. 141 (1925).

The Scottish courts have consistently allowed recovery for disability due to nervous shock, negligently caused, without requiring any impact. Cooper v. Caledonian Ry., (1902) 4 F. 880, Ct. of Sess.; Gilligan v. Robb, (1910) S.C. 856, Ct. of Sess.; Coyle v. Watson, (1915) A.C. 1; Brown v. Glasgow Corp., (1922) S.C. 527, Ct. of Sess.; Currie v. Wardrop, (1927) Scottish Law Times 383.

[7] Courts of the following American states allow recovery for injury or disability due to psychic stimuli, negligently caused by defendant, without necessity for proving physical impact:

Ala. Alabama Fuel & Iron Co. v. Baladoni, 15 Ala. App. 316, 73 So. 205 (1916).
Cal. Lindley v. Knowlton, 179 Cal. 298, 176 Pac. 440 (1918).
Ga. Goddard v. Watters, 14 Ga. App. 722, 82 S.E. 304 (1914).
Ia. Watson v. Dilts, 116 Iowa 249, 89 N.W. 1068 (1902).
Kan. Whitsell v. Watts, 98 Kan. 508, 159 Pac. 401 (1916).
La. Stewart v. Arkansas Southern R. Co., 112 La. 764, 36 So. 676 (1904).
Md. Green v. Shoemaker, 111 Md. 69, 73 Atl. 688 (1909).
Minn. Purcell v. St. Paul City R. Co., 48 Minn. 34, 50 N.W. 1034 (1892).
Neb. Hanford v. Omaha Street R. Co., 113 Neb. 423, 203 N.W. 643 (1925).
N. H. Chinchiolo v. New England Wholesale Tailors, 84 N. H. 329, 150 Atl. 540 (1930).
N. C. Kimberly v. Howland, 143 N. C. 398, 55 S.E. 778 (1906).
Ore. Salmi v. Columbia, etc. R. Co., 75 Ore. 200, 146 Pac. 819 (1915).
R. I. Simone v. Rhode Island Co., 28 R. I. 186, 66 Atl. 202 (1907).
S. C. Mack v. South-Bound R. Co., 52 S. C. 323, 29 S.E. 905 (1897).

Other courts, of which Massachusetts, New York and Pennsylvania are noteworthy examples, have felt that some further guarantee is necessary. This is satisfied if contemporaneously with the emotional stimulus, such as fright, the defendant by his negligence also causes an impact against the plaintiff's body. This was an attractive and plausible device, to the legal mind, for letting down the bars against recovery of damages. In the first place, as we have seen, the negligent impact itself would give the plaintiff an independent cause of action for at least some damages, and this enabled the courts to make use of the historical custom of tacking on "parasitic damages" as a means of compensating consequences of "nervous shock." Secondly, it was felt that the defendant as actor was here more culpable in terms of fault. Thirdly, some guarantee against simulation or fraud would exist, if the plaintiff had to prove actual impact, as this would tend to verify the fact that plaintiff was actually present at the scene of the accident and within the range of defendant's stimulus. Fourthly, in the first promulgation of this doctrine, there was doubtless a bona fide supposition that the impact would be severe enough so that one could not say what part of the "nervous shock" was due to the blow and what part was due to the psychic stimulus. It was easy to reason that the law need not be tender with the wrong-doer, and an exact scientific method of proof would not be insisted upon. This is what we may well characterize as the purely pragmatic approach early adopted by the Massachusetts courts. The essential position of these jurisdictions is that no analytical ground in tort law can be found for a blanket refusal of liability in cases of "injury without impact," but that practical considerations of policy and proof make it necessary to refuse recovery unless plaintiff can prove some contemporaneous impact.[8]

Presence or absence of impact can have no justifiable relation to the matter unless the courts further require that the physical impact be of such character that it can produce a substantial part of the nervous shock. In

S. D. Sternhagen v. Kozel, 40 S. D. 396, 167 N.W. 398 (1918).
Tenn. Memphis St. R. Co. v. Bernstein, 137 Tenn. 627, 194 S.W. 902 (1917).
Tex. Gulf, etc. R. Co. v. Hayter, 93 Tex. 239, 54 S.W. 944 (1900).
Wash. O'Meara v. Russell, 90 Wash. 557, 156 Pac. 550 (1916).
Wis. Pankopf v. Hinkley, 141 Wis. 146, 123 N.W. 625 (1909).

[8] Courts of the following American states deny recovery for injury due to fright or other psychic stimuli, negligently caused by defendant, if there is no contemporaneous physical impact:

U. S. Haile's Curator v. Texas & Pacific R. Co. (U. S. Cir. Ct. of App., Fifth Cir.), 60 Fed. 557 (1894). (Federal courts now must follow the tort law of the state in which they are situated.)
Ark. St. Louis, etc. R. Co. v. Bragg, 69 Ark. 402, 64 S.W. 226 (1901).
Ill. Braun v. Craven, 175 Ill. 401, 51 N.E. 657 (1898).
Ind. Terre Haute Electric R. Co. v. Lauer, 21 Ind. App. 466, 52 N.E. 703 (1899).
Ky. McGee v. Vanover, 148 Ky. 737, 147 S.W. 742 (1912).
Mass. Spade v. Lynn, etc. R. Co., 168 Mass. 285, 47 N.E. 88 (1897).
Mich. Nelson v. Crawford, 122 Mich. 466, 81 N.W. 335 (1899).
Mo. McArdle v. Peck Dry Goods Co., 191 Mo. App. 263, 177 S.W. 1095 (1915).
N. J. Ward v. West Jersey, etc. R. Co., 65 N. J. L. 383, 47 Atl. 561 (1900).
N. Y. Mitchell v. Rochester Ry. Co., 151 N. Y. 107, 45 N.E. 354 (1896).
O. Miller v. Baltimore, etc. R. Co., 78 Oh. St. 309, 85 N.E. 499 (1908).
Pa. Ewing v. Pittsburgh, etc. R. Co., 147 Pa. St. 40, 23 Atl. 340 (1892).

practice, those courts which started out bravely to espouse the position that there can be no recovery for 'injury without impact' because of the likely promotion of fraud, have themselves prostituted their ideal. Inspection of the cases in the various jurisdictions shows that today the most trivial impact is held adequate to enable a recovery. For instance, the Massachusetts courts first held that a superficial bruise was enough,[9] and later went to the extreme of holding that a mere impact without visible discoloration would suffice, for one could not say that the impact did not cause internal injury.[10]

This tendency to make of "impact" a mere nominal prerequisite to a right of action for nervous shock is seen in the decisions of practically all the courts which follow the minority view. In the recent New York case of Comstock v. Wilson,[11] plaintiff was riding with her husband when the defendant negligently struck the back of their car with his own machine. The collision was a minor one, but it produced some noise or "grating sound" without inflicting any personal injury. One could not very well predicate more than a slight impact due to jarring of decedent as she sat in her husband's car. She promptly stepped from the car and started to write down the defendant's name and license number, all within a few minutes of the accident. While so doing she fainted and fell to the sidewalk, fracturing her skull and died within 20 minutes of that time. Decedent's husband brought an action for damages against defendant and recovered a verdict in the trial court for $5,000. On appeal this was affirmed. The court held that the slight jarring of decedent was sufficient to satisfy the requirement of an "impact."

Obviously, the test of "impact" has become a mere formal requisite, and on that ground the minority courts have been severely criticized for not dispensing with it altogether. As things now stand, plaintiffs in the minority

[9] Driscoll v. Gaffey, 207 Mass. 102, 92 N.E. 1010 (1910). (Defendant's negligent blasting caused a 20 pound stone to be thrown on P's house with a loud noise; P was frightened and fell to the floor receiving only a superficial bruise. Held: This impact was injurious enough to permit recovery for neurasthenia attributed by doctors to contemporaneous fright.)

[10] Kisiel v. Holyoke Street Railway Co., 240 Mass. 29, 132 N.E. 622 (1921). (Plaintiff, a pregnant woman, while a passenger on D's street car, was slightly jarred by a negligent rear end collision with another of D's cars, and she alleged that fright caused an abortion. Held, affirming judgment for plaintiff entered on jury verdict: The impact was sufficient; though the bump may have produced no outwardly visible physical injury, it may have produced internal injury.) Note, that in Freedman v. Eastern Mass. Street Ry. Co., 299 Mass. 246, 12 N.E. (2d) 739 (1938), the Supreme Judicial Court of Massachusetts definitely makes the requirement for recovery, "physical injury from without" as contrasted with injury due to "the purely internal operation of fright." Plaintiff, a passenger on D's street car, was so frightened by a negligent side to side collision with a truck that she jumped from her seat and in so doing twisted her shoulder. The trial court directed a verdict for defendant because there was no proof of an impact. Held: Such proof is not necessary where, as here, defendant's negligence causes physical injury from without.

Comment: At first this distinction may seem tenuous, but it is substantial in terms of making proof. Most other courts have held that if A creates in B a reasonable apprehension of bodily peril, and B injures himself in trying to escape the danger, he can hold B in damages, even though fear was a link in the chain of causation. The injury is physical (broken leg, etc.) and immediate, and there is no such difficulty with conjectural causation as one finds in the usual nervous shock cases.

[11] 257 N. Y. 231, 177 N.E. 431 (1931).

jurisdictions have every inducement to claim some fanciful or fraudulent impact in order to gain a right to recover for "nervous shock." The frauds which the court hoped to hold out by closing the door have crept in through the open window.

As a matter of fact, there was a great deal of practical force and merit in the original refusal of the Coultas case (Eng.) and of the Spade and Homans cases (Mass.) to allow recovery in the "nervous shock" cases on the supposition that more frauds would be encouraged by an opposite rule than meritorious cases cut off. The systematic study of the relations of emotions to injury and disease did not begin until about 1929 when Cannon [15] published his book. Previously many assertions made in court regarding disease or injury caused by fright or other psychic stimuli involved more supposition and conjecture than systematized knowledge or experience of the medical profession. Our impression from considering a great number of the legal decisions is that the "impact" requirement as a guarantee of merit has utterly failed in its purpose of filtering out valid claims for "nervous shock" from shabby ones. The attempt of the courts to press into service such a simple sifting device was fore-doomed to failure, for it had no scientific basis. Probably it is true that until recently the balance of justice and equity would have been served by refusing recovery in ordinary cases of "nervous shock" in accordance with the premonition of the Coultas case.

Inspection of the decided cases shows a hopeless lack of any scientific criteria in assessing the merit of particular claims. It is interesting to find that the appeal courts are completely unable at present to appraise the sufficiency of proof of causation. The result is that any doctor who is willing to do so can put forward a categorical opinion to the effect that causation of the alleged injury has medical support, and thus make a case for the jury, when the opinion represents sheer personal speculation and conjecture.

We hasten to add, however, that we are now gaining the medical knowledge necessary to enable a fair appraisal of these claims. Psychosomatic medicine is bringing together with beneficial convergence this whole series of problems regarding what injuries or diseases may be caused by emotional stimuli. Though until recently the balance of arguments was with the Coultas view denying liability (despite adverse criticism of law writers), the augmentation of scientific knowledge has altered the situation. All courts should now recognize a right of action for "injury without impact," on the ground that the old practical arguments against allowing a right of action have lost their force, since we are in position to supply scientific criteria of validity heretofore not available. The minority jurisdictions should shift their view in keeping with this new scientific accession of knowledge. They may do this either by renouncing past decisions, or by taking up a new definition of "impact" as suggested in our initial footnote, recognizing that "nervous shock" always involves impact although the sensory bombardment may be through sound, light or heat waves. A more valuable guarantee of actual causation of the injury by the stimulus would be to insist upon im-

mediate appearance of the harm or of satisfactory "bridging" symptoms to fill the interval between stimulus and alleged response.

It is the purpose of this paper to put forward a rationale of "nervous shock" and its possible consequences which may have some value as criteria of scientific proof, both for the expert witness and for courts.

II. Consideration of "Nervous Shock" and of Injuries and Diseases Which May Result Therefrom

We find from reviewing the law cases that the most numerous claims for injury or disease caused by psychic stimuli fall into these groups:

(1) Miscarriage or abortion.[12]

(2) "Traumatic neuroses." This condition is included because in a majority of cases the impact is not a substantial cause of the neurosis but only an occasion for the expression of symptoms.[13]

(3) "Nervous shock," allegedly resulting in disability, injury or disease. In our discussion we exclude all those cases where there has been a mere transient disturbance of emotional or mental tranquillity, rapidly disappearing without resultant disability. It is not surprising to find that the important psychic stimulant which the plaintiff seeks to incriminate in the majority of these cases is fright, for that is the emotion most likely to be engendered by realization of sudden peril or danger. Usually the defendant has negligently brought a railway locomotive or some other dangerous force into close proximity with plaintiff, so as to threaten some immediate bodily harm, and this gives rise to the plaintiff's emotional response.

Since we propose to leave the first two categories of claims to others for discussion, it seems appropriate that we give a clinical characterization of "nervous shock" and the mechanism of its action, before proceeding to suggest a definite legal rationale for disposing of individual cases.

Definitions

Emotional states are difficult to define, because they have both a subjective and objective aspect.[14] They are complex reactions in the human animal, reactions that arise in response to environmental stimulation or the memory thereof. The subjective part is an acute awareness of various bodily sensations and diffuse feelings not easily referable to any organ; the aroused awareness itself is an important part of the picture. The objective part of emotion is that which is seen when one observes critically a person suffering emotional stress, e.g., the muscular tension, motor restlessness, tremor, expressive intonation of voice, wide pupils, sweating, pallor of face, cold hands and all the other autonomic reactions described by Cannon as preparation

[12] These cases are very numerous and criteria of proof are needed for both traumatic and psychic abortion. Because the subject, in its details, calls for special treatment, we exclude it from the present study. See Hertig and Sheldon, Minimum criteria required to prove prima facie case of traumatic abortion or miscarriage, *in* Smith on Scientific Proof and Relations of Law and Medicine, Albany, N. Y., Matthew Bender & Co., (In press).

[13] See Smith, H. W., and Solomon, H. C.: Traumatic neuroses in court, *in* Smith on Scientific Proof and Relations of Law and Medicine, *id.*

[14] Bridges, J. W.: Outline of abnormal psychology, 1931, R. G. Adams & Co., Columbus.

for emergency. Emotions are commonly classified as Fear, Rage, Grief, Loneliness and Love, with many subdivisions. The old theory of James and Lange, that emotions (the subjective part) are the result of the visceral changes (objective part), is no longer tenable. Cannon [15] has demonstrated that animals can show signs of emotion when the viscera are separated from the brain by cutting the autonomic nerves.

Injury is used in this paper as meaning harmful changes in the organism caused by environmental forces of a mechanical nature. The evidence for these changes may be either the detection of abnormal functions or the seeing of lesions. A lesion is defined as visible abnormality of tissue in contrast to submicroscopical and chemical changes in structure. The naive dichotomy "organic vs. functional" is denied.

Disease is the process which causes all harmful changes in the organism other then those caused by injury.

Psychosomatic medicine includes, strictly speaking, any branch of medicine where both psychology and physiology are concerned. The body or "soma" is the whole of the organism except the reproductive cells. The *"psyche"* is the result of function of the more highly integrated parts of the central nervous system; the functions that are commonly considered "psychological." [16] Since all organs are more or less controlled by the nerves that run to them from the central nervous system, and since psychological functions might effect such control, all medicine might be considered "psychosomatic." From a practical standpoint, however, one must consider "psychosomatics" as of 1943; just now it is a field of clinical medicine that is attracting much attention because new knowledge in psychology and in clinical medicine indicates the psychogenesis of many symptoms (abnormalities of function) and even of some lesions. In short "psychosomatic medicine" is the clinical field where the internist or medical specialist can help the psychiatrist, and where the psychiatrist can help the medical man in the study and treatment of disease.

The Evidence That Emotions May Cause Disorders of Function. Observations on the effect of the emotions upon the bodily functions are as old as medical science and as varied as the combinations of personalities and situations would mathematically suggest. Nevertheless, certain combinations have occurred over and over again, and these have become recognized clinical "facts." The evidence is convincing to most medical men that there is a cause and effect relation between the emotional stress and the symptoms, but the phenomena are striking only because of common occurrence. The "proof" that they are causally connected is only of the *"post hoc ergo propter hoc"* variety; no physiological mechanisms, no series of pathological processes are known to explain the symptoms. There is so much of this clinical observation that it cannot all be discussed in a single paper; it fills volumes in the literature. Three recent books probably summarize it satisfactorily. The most recent and thorough is Dunbar's "Emotions and Bodily Changes." [17] Here one may find a great number of clinical examples abstracted from 2251 different contributions. Much of it is only expression of opinion, but there is a great deal of good observation that cannot be ignored. In 1930 Leopold Alkan published an important book "Ana-

[15] CANNON, W. B.: Bodily changes in pain, hunger, fear and rage, 1929, Appleton & Co., New York.

[16] COBB, S.: Borderlands of psychiatry, 1943, Harvard University Press, Cambridge, Mass.

[17] DUNBAR, H. F.: Emotions and bodily changes, 1935, Columbia University Press, New York.

tomische Organkrankheiten aus seelischer Ursache" [18] in which he shows how motor disturbances of hollow organs and tubular organs can lead to spasms with resulting stasis, infection and necrosis. He also shows how secretions of glands may be affected by nervous stimulation to cause symptoms. This book is based on clinical observations. It is interesting reading but the author seems a little too ready to accept an interesting combination of circumstances as proof for a theory.

The third book is Fritz Mohr's "Psychophysische Behandlungsmethoden," [19] which gives evidence of a different kind. He tells of 20 years' experience in "curing" people, i.e., removing symptoms by psychological methods. It is a good contribution, although evidence of this sort can often be interpreted in more than one way.

Modern "Psychosomatics" may be said to have really begun with Walter B. Cannon, when he published his book "Bodily Changes in Hunger, Fear, Pain and Rage." [15] Pavlov and others had given physiological evidence of such mechanisms, but Cannon brought the subject to an issue and formulated a theory which has profoundly affected the thinking of physicians and psychiatrists throughout the world. In his second great book "The Wisdom of the Body" [20] Cannon sums up the responses of an animal to powerful emotion as follows:

> It is remarkable that most of these reactions occur as the accompaniment of the powerful emotions of rage and fear. Respiration deepens, the heart beats more rapidly, the arterial pressure rises, the blood is shifted away from the stomach and intestines to the heart and central nervous system and the muscles, the processes in the alimentary canal cease, sugar is freed from the reserves in the liver, the spleen contracts and discharges its content of concentrated corpuscles, and adrenin is secreted from the adrenal medulla.
>
> The emotional responses just listed may reasonably be regarded as preparatory for struggle. They are adjustments which, so far as possible, put the organism in readiness for meeting the demands which will be made upon it. The secreted adrenin cooperates with sympathetic nerve impulses in calling forth stored glycogen from the liver, thus flooding the blood with sugar for the use of laboring muscles; it helps in distributing the blood in abundance to the heart, the brain, and the limbs (i.e., to the parts essential for intense physical effort) while taking it away from the inhibited organs in the abdomen; it quickly abolishes the effects of muscular fatigue so that the organism which can muster adrenin in the blood can restore to its tired muscles the same readiness to act which they had when fresh; and it renders the blood more rapidly coagulable. The increased respiration, the redistributed blood running at high pressure, and the more numerous red corpuscles set free from the spleen provide for essential oxygen and for riddance of acid waste, and make a setting for instantaneous and supreme action. In short, all these changes are directly serviceable in rendering the organism more effective in the violent display of energy which fear or rage may involve.

Taking the systems and organs mentioned by Cannon as responding physiologically to fear and rage, one can make a table showing the disorders of

[18] ALKAN, L.: Anatomische Organkrankheiten aus seelischer Ursache, 1930, Hippokrates, Stuttgart.
[19] MOHR, F.: Psycho-physische Behandlungsmethoden, 1925, Hirzel, Leipzig.
[20] CANNON, W. B.: Wisdom of the body, 1932, Norton, New York.

these systems best known to accompany emotional stress in man. We do not assert that the emotional stress is the primary or sole cause of these disorders, though in some instances this may be true, but rather that emotions may excite an attack or aggravate one already in progress. Only those disorders are listed for which there is abundant clinical evidence.

TABLE OF CLINICAL DISORDERS PROBABLY RELATED TO EMOTIONAL STIMULATION

Arranged by systems and followed by a good reference which has adequate bibliography. Emotions may be related to the diseases listed as (1) exciting causes of an attack or (2) aggravating factors after an attack is started. Both would apply to all the diseases. A single powerful stimulus has been known to produce an attack in those marked (S) although usually a long bombardment with emotional stimuli is needed.

Respiratory System	
Bronchial asthma (S)	French and Alexander [21]
Hyperventilation tetany (S)	Talbott, Cobb, et al [22]
DaCosta's syndrome (S)	Wood [23]
Cardiovascular System	
Angina pectoris (S)	Fahrenkamp [24]
Hypertension (S)	Weiss [25]
Neurocirculatory asthenia (S)	Wood [23]
Muscular and Skeletal Systems	
Rheumatoid arthritis	Cobb, Bauer, Whiting [26]
Tremors and contractures (S)	Babinski and Froment [27]
Alimentary (Gastrointestinal) System	
Mucous colitis (S)	White, Cobb, Jones [28]
Peptic ulcer	Wolf, Wolff [29]
Dyspepsia and "gastritis" (S)	Mittelmann and Wolff [30]
Genitourinary System	
Retention of urine (S)	Schwarz [31]
Enuresis (S)	Michaels [32]
Impotence (S)	Schwarz [31]
Dysmenorrhea (S)	Novak, Harrik [33]
Endocrine System	
Thyrotoxicosis (Basedow or Graves' Disease) (S)	Mittelmann [34]
Diabetes Mellitus	Liebig [35]
Anorexia Nervosa	Richardson [36]
Integument (skin)	
Neurodermatitis (S)	Greenhill, Finesinger [37]
Psoriasis	Bunnemann [38]

[21] FRENCH, T. M., and ALEXANDER, F.: Psychogenic factors in bronchial asthma, Psychosom. Med. Monogr., 1941, II and IV.

[22] TALBOTT, J. H., COBB, S., COOMBS, F. S., COHEN, M. E., and CONSOLAZIO, W. W.: Acid-base balance of the blood in a patient with hysterical hyperventilation, Arch. Neurol. and Psychiat., 1938, xxxviii, 973.

[23] WOOD, P.: DaCosta's syndrome (or effort syndrome), Brit. Med. Jr., 1941, i, 767, 805, 845.

[24] FAHRENKAMP, K.: Der Herzkranke, 1931, Hippokrates, Stuttgart.

[25] WEISS, E.: Cardiovascular lesions of probable origin in arterial hypertension, Psychosom. Med., 1940, ii, 249.

[26] COBB, S., BAUER, W., and WHITING, I.: Environmental factors in rheumatoid arthritis, Jr. Am. Med. Assoc., 1939, cxiii, 668.

[27] BABINSKI, J., and FROMENT, J.: Hysteria or pithiatism, 1918, University of London, London.

[28] WHITE, B. V., COBB, S., and JONES, C. M.: Mucous colitis, Psychosom. Med. Monogr., 1939, I.

[29] WOLF, S., and WOLFF, H. G.: Genesis of peptic ulcer in man, Jr. Am. Med. Assoc., 1942, cxx, 670.

[30] MITTELMANN, B., and WOLFF, H. G.: Emotions and gastroduodenal function; experimental studies on patients with gastritis, duodenitis and peptic ulcer, Psychosom. Med., 1942, iv, 5.

The nervous system is not included in the table because it functions largely as an intermediary mechanism for the conduction of nerve impulses from sense organ or to muscles and glands. The nervous system, especially the autonomic nervous system, acts as a pathway, not as an organ system. It is the behavior of those muscles and glands that make the symptoms discussed under each of the headings above. The muscles involved are mostly the smooth muscles of blood vessels and viscera, but the skeletal muscles may be involved. The psychological phenomena stimulated by emotions can hardly be called psychosomatic; they are psychiatric problems.

The proposition that the symptoms found in the various disorders listed are mostly the result of hyperfunction of the autonomic nervous system can be illustrated by many clinical observations. For example, fear or anger when excessive causes pallor and relaxation of the stomach, whereas anxiety and recurrent annoyances cause hypermotility, hyperemia and hypersecretion. Spasm of blood vessels causes people to become "pale-with-emotion" in the face, hands and stomach. Different degrees of emotion or different personal reactions can cause flushing of the face, neck and rectum.[39] Vomiting and urgent urination are common accompaniments of fear. Thus, Cannon's concept of sympathetic stimulation as a reaction to fear and preparation for flight or fight, is a useful basis for the understanding of many, if not most psychosomatic disorders. The endocrine glands and the autonomic nervous system are the great mediators between psyche and soma. Through them emotions are *expressed* (sic) as normal actions or symptoms.

Of course it is arbitrary to make a distinction between a disorder of function and a disorder of structure. It is a naïve idea arising from the good old days when only "seeing was believing." Unfortunately it has led to a common but harmful clinical slang which divides all disease into "functional" or "organic." In this slang "functional" is not used in the physiological sense (or it would include all symptoms) and "organic" is loosely thought to mean a "structural" change or "lesion." Any scientist should know nowadays that a chemical change is just as "structural" as a lesion

[31] SCHWARTZ, O.: Psychogenese und Psychotherapie körperlicher Symptome, 1925, Springer, Berlin.

[32] MICHAELS, J. J., and GOODMAN, S. E.: Enuresis and other factors in normal and in psychotic persons; comparative study of incidence and intercorrelations, Arch. Neurol. and Psychiat., 1938, xl, 699.

[33] NOVAK, J., and HARNIK, M.: Die psychogene Entstehung der Menstrualkolik und deren Behandlung, Ztschr. f. Geburtsh. u. Gynäk., 1929, xcvi, 239.

[34] MITTELMANN, B.: Psychogenic factors and psychotherapy in hyperthyreosis and rapid heart imbalance, Jr. Nerv. and Ment. Dis., 1933, lxxvii, 465.

[35] LIEBIG, H.: Trauma und Diabetes mellitus, Med. Klin., 1932, xxviii, 357.

[36] RAHMAN, L., RICHARDSON, H. B., and RIPLEY, H. S.: Anorexia nervosa with psychiatric observations, Psychosomat. Med., 1939, i, 335.

[37] GREENHILL, M. H., and FINESINGER, J. E.: Neurotic symptoms and emotional factors in atopic dermatitis, Arch. Dermat. and Syph., 1942, xlvi, 187.

[38] BUNNEMANN, O.: Neue Beiträge zur Frage der Psychogenese von Hautsymptomen, Ztschr. f. d. ges. Neurol. u. Psychiat., 1924, lxxxviii, 589.

[39] WHITE, B. V., and JONES, C. M.: Effect of irritants and drugs affecting the autonomic nervous system upon the mucosa of the normal rectum and rectosigmoid with especial reference to "mucous colitis," New England Jr. Med., 1938, ccxviii, 791.

caused with an axe. There can be no line between structure and function, between an organ at rest and an organ in action. For convenience and to avoid the stultifying conception of the dichotomies "organic or functional," "physical or mental" diseases should be considered as arising from at least four sources: hereditary (genogenic), chemical (chemogenic), visible tissue damage (histogenic) and psychological disorders (psychogenic).[40]

The Evidence That Lesions May Be Caused by Emotional Trauma. (*a*) Psychogenic lesions appearing in apparently healthy persons. The basic observation that leads on to all other considerations of psychogenic lesions is that a blister can be raised on the skin by hypnotic suggestion and removed by the same means. Three competent observers with expert witnesses have reported that this can happen—Kreibrik (1907), Kohnstmann and Pinner (1908), and Schindler (1927). The latter wrote a monograph in which he describes not only blisters, but subcutaneous hemorrhages caused by hypnosis and eliminated by hypnosis.[41] Dunbar [17] reviews the literature and gives several other references.

The reason this is spoken of as the basic observation is because it is direct, with no complicating steps that need explanation. If it is accepted as a fact many psychogenic phenomena become credible, and the great variety of clinical phenomena (listed above) have a plausible origin in emotional stress.

A more complicated series of events, but one that is now well proved by the work of Wolff [29] is that leading to peptic ulcer. His preliminary studies on gastric motility and reaction in relation to emotional stimuli [30] gave presumptive evidence that peptic ulcer could arise from nervous tension. His recent remarkable studies on a man with a gastrostomy seem to prove the relationship. The mucosa of this man's stomach could be seen through the artificial mouth. When he was anxious and resentful, there was increased acid secretion, the mucosa became hyperemic and motility increased. If these changes were severe and continued, small hemorrhages appeared beneath the mucous membrane, causing erosion of the surface. In a few instances when the acid hypersecretion was not kept away from the surface of the mucous membrane by the protective layer of mucous, a chronic ulcer developed. In Wolff's [29] words: "it appears likely, then, that the chain of events which begins with anxiety and conflict and their associated overactivity of the stomach and ends with hemorrhage or perforation is that which is involved in the natural history of peptic ulcer in human beings."

In cardiospasm [18] a somewhat similar mechanism is seen. At the cardiac end of the stomach, just below the esophagus a spasm of muscle may take place when the patient is emotionally upset. This closes the entrance to the stomach, saliva, mucous and food collect in the esophagus, vomiting occurs, and the lower part of the esophagus is dilated and often shows erosions and infection of the mucous membrane. In chronic cases these lesions (fusiform dilatation, mucosal erosion) are seen at autopsy but the ring of muscle

[40] COBB, S.: Foundations of neuropsychiatry, 1941, Williams and Wilkins, Baltimore.
[41] SCHINDLER, R.: Nervensystem und spontane Blutungen, 1927, Karger, Berlin.

at the cardia, that caused them by its obstructive spasm, has relaxed in death and appears normal.

A quite different sort of lesion is found in cases of hysterical paralysis of long duration.[27] The unused muscles become atrophied and fibrotic holding the limb almost immobile by the muscular contractures. These muscular lesions, however, can be considered a secondary result through disuse; some direct trophic change in the muscle, however, is a possibility.

(*b*) Psychogenic lesions appearing in patients with an hereditary predisposition. Persons who appear healthy and normal may yet be unusually susceptible to emotional shock because of an inherited instability of certain organ-systems. Perhaps the best example is what Means [42] describes as the patient who is like a "loaded gun"; she has inherited a tendency to thyrotoxicosis, and when a severe emotional trauma comes into her life, it, so to speak, "pulls the trigger" and the full blown syndrome of Graves' disease can appear in 48 hours, with exophthalmos, enlarged thyroid and increased metabolic rate; later hypertrophy of the thyroid may develop and myocardial damage. There are so many cases cited that only two references will be given to especially striking reports.[43, 44]

Raynaud's disease is another good example of psychogenic lesions appearing in a susceptible person. In these patients there is probably an inherited tendency to spasm in the small vessels of the hands and feet causing cold and white extremities. In marked cases these vascular spasms lead to such prolonged asphyxia of the tissues that necrosis results, with ulceration appearing on the fingers or toes. The onset of the spasms of the small vessels has been observed under the microscope, and seen to occur in definite relationship to emotional stimulation.[45, 46] White hands or fingers often occur in these patients immediately after emotional stress, and if the situation is prolonged the ulcerations appear.[47]

(*c*) Psychogenic increase of lesions already present. The killing of patients with angina pectoris by emotional excitement is an everyday occurrence. It is said that every radio broadcast of a prize-fight has several "cardiac" victims. In these cases the blood supply to the heart is already decreased by disease of the coronary arteries and a spasm of these vessels set up by emotional stimulation may cause an infarct of the heart muscle with focal necrosis and stoppage of the heart.[48]

[42] MEANS, J. H.: Thyroid and its diseases, 1937, Lippincott Co., Philadelphia.

[43] RAHM, H.: Zur Pathogenese und Therapie des Morbus Basedow, Nervenarzt, 1930, iii, 1.

[44] ROUSSY, G., and CORNIL, L.: La maladie de Basedow et la guerre, Presse méd., 1920, xxviii, 753.

[45] FREMONT-SMITH, F.: Personal communication.

[46] DEUTSCH, F.: Capillary studies in Raynaud's disease, Jr. Lab. and Clin. Med., 1941, xxvi, 1729.

[47] COBB, S.: Borderlands of psychiatry, case No. 1, Ch. I, 1943, Harvard Univ. Press, Cambridge, Mass.

[48] WHITE, P. D.: Scientific Proof in Respect to Injuries of the Heart, in Smith on Scientific Proof and Relations of Law and Medicine, Matthew Bender & Co., Albany, N. Y., in press.

Several other types of immediate death due to emotional shock or psychological disorder have been described, but in none except angina pectoris is the mechanism simple and direct enough to constitute proof.

III. Rationale for the "Nervous Shock" Cases

In developing a rationale for the nervous shock cases, it is not possible to divorce scientific considerations from legal theory. It is useful, in arriving at the legal components of this problem, to bear constantly in mind the essential ingredients of any cause of action.

A plaintiff who seeks to recover money damages in a court of law has the burden of proof to establish, by a preponderance of substantial evidence, the concurrent existence of the following four factors, namely: Duty $\overrightarrow{+}$ Dereliction $\overrightarrow{+}$ Proximate Causation $\rightarrow$ Injury. If he fails to offer such evidence in respect to any of these four necessary ingredients, he fails to establish a *prima facie* cause of action. In that event, the defendant on timely motion is entitled to have the trial court instruct the jury to return a verdict against the plaintiff and in favor of the defendant. If this be done, and judgment is entered on the verdict and thereafter becomes final, the plaintiff is forever barred from further maintaining an action for the same alleged grievance. It is obviously pertinent to our theme, to consider what bearing each of the four terms mentioned may have on the making out of a cause of action for nervous shock. To this end we shall consider each term in seriatim.

A. Duty-Dereliction.

1. *Basis of liability and standard of care.* Duty and dereliction are so closely linked in the law of torts that they are logically like reverse faces of the same coin. It is convenient, however, to think of duty as the pervasive obligation which every member of society owes to avoid creating a substantial risk of injury to those whom he knows or should know are within his sphere of action. It is helpful to characterize this surrounding orbit as the circle of risk. No individual owes a duty to act in respect to another person unless such obligation has been cast upon him by a preëxisting contract or special relationship. In the usual negligence case, where actor and person acted upon are strangers, we are not able to find a preëxisting special duty, and it is necessary to plaintiff's proof of a cause of action that he show some affirmative conduct creating an unreasonable risk of injury to persons of plaintiff's class. In defining what is negligent conduct and what is due care, we take as our standard of reference what the average prudent man would have done under like circumstances.

a. What degree of protection shall the law vouchsafe to the idiosyncratic or excessively vulnerable person? Society has an interest in promoting legitimate enterprise and in encouraging the prime mover. It is also interested in protecting, by way of restitution through money awards, persons who may be injured by the conduct of the actor. These competing interests

are of distinct materiality in the law of torts, which in the last analysis is concerned with placing the risk of loss or injury equitably as between plaintiff and defendant.[49] The law of torts makes use of the concept of culpability or fault, as contrasted with mere causation in determining whether the actor shall make compensation to the person acted upon. Culpability may consist of intentional wrongdoing, and thus partake of a malicious character, or it may consist only of negligence akin to inadvertence. The person acted upon may possess either an average constitution, or he may be an idiosyncratic person who reacts excessively to minimal stimulation. The test of whether an actor, in exercise of due care,* should foresee the likelihood of some injury to another person in the circle of risk must also take into account the nature of the stimulus or conduct and its adequacy to produce injury under normal circumstances. It is only where the actor has reason to foresee some injury to others in his environment that we can justly expect him to abstain from going forward with his legitimate affairs, or can equitably place any liability upon him to pay for injury to others.

It is fair, in our opinion, to hold that an actor has no greater duty of care to one who is idiosyncratic or excessively vulnerable to injury than he owes in respect to normally constituted persons, unless he knows of the idiosyncrasy in advance, or commits an intentional wrong rather than a merely negligent act.

(1) *If the psychic stimulus created by the defendant actor would not have effected an injurious response in a person of normal constitution, there is no breach of duty to one whose injury flows from an idiosyncrasy unknown to the actor.*

Example: D, a woman, had gone to the home of P to help pick and can peaches. A difference of opinion arose between the pickers as to what peaches should be used. In connection with this dispute, D went into the house where P was in bed, and according to P's version, D "wilfully talked in a loud voice and in an angry manner with divers persons in the hearing of the plaintiff." D was unaware that P had been subject to hysteria in times past and was hypersensitive. P sued D, alleging that her loud and angry address had caused P to have hysterial spells on the day in question and one about every 30 days thereafter. P recovered verdict and judgment in the trial court for $100.

Held, on appeal: Judgment reversed; P cannot recover for the reason that D breached no duty of care to her, having no ground to anticipate that P would react excessively to a stimulus innocuous to an average person. Furthermore, "the injury in question not being one which the defendant could reasonably be expected to

[49] In connection with this argument for limiting extent of tort liability to idiosyncratic or hypersensitive persons, in respect to mere negligence, see SMITH, H. W., and SOLOMON, H. C.: Traumatic neuroses in Court, *op. cit. supra* fn. 13. See also POUND, R.: Interests of personality, 28 Harvard Law Rev. (1915) 343, 445.

* Due care is defined by an *objective* test, namely: Did the actor use that degree of care (care, diligence, skill and judgment) which the average prudent man would have used under the same or similar circumstances to avoid creating risk of injury by his conduct to those persons or things within range of the peril, whose presence he knew or should have foreseen prior to indulging his conduct?

anticipate as likely to ensue from her conduct, we cannot regard it as the natural consequence thereof for which defendant is legally responsible."

Haas v. Metz, 78 Ill. App. 46 (1898).

(2) *If in advance of the action the actor becomes aware of the idiosyncrasy of some person in the sphere of action, or should know of it, the ordinary duty to use due care may require the actor to abstain from creating or continuing a stimulus which would not hurt the normal person but carries a substantial risk of injury to the vulnerable individual* (see footnote 67, post).

(3) *If the defendant commits an intentional invasion of the plaintiff's rights of personality, he assumes the risk of special vulnerability of the person acted upon.* In this situation, the actor "takes his victim as he finds him" for the reason that the law has no cause for balancing interests or making concessions on behalf of the actor.

Example: Defendant, while in his own house, fired several shots through the lighted window of plaintiff's apartment. P had given birth to a child a few minutes before and was in a hypersensitive condition, unknown to D. She was not struck but she reacted violently and suffered extreme fright, nervous shock, and hysteria, resulting in serious illness. P sued D, but the trial court dismissed the petition on the ground that the New York rule laid down in Mitchell v. Rochester Ry. Co., 151 N. Y. 107, 45 N.E. 354 (1896), denies recovery of damages for injury due to nervous shock or fright unless the plaintiff can prove a contemporaneous impact.

Held, on appeal: Judgment reversed. The defendant indulged willful and wanton conduct, whether it be technically characterized as an assault or not. For injuries sustained thereby as a result of fright, P is entitled to recover her full damages. The Mitchell case applies only to accidents based on negligence, and not to cases of willful tort.

Beck v. Libraro, 220 App. Div. 547, 221 N. Y. Supp. 737 (1927).

(4) *If the conduct is negligent in creating a risk of injury to normally constituted persons, the idiosyncratic individual is allowed to recover full damages for his excessive response, excluding, however, any allowance for preëxisting impairment.*

2. *Test of culpability in the nervous shock cases.* Not only is it important to consider whether the culpability involved an intentional and malicious act or mere negligence, and whether the person affected was of normal or idiosyncratic constitution, but one must take into account the adequacy of the stimulus. It is believed that in many of the negligence cases involving nervous shock, the trial courts have not made the importance of this factor sufficiently clear to the jury. The trial court should charge the jury at the conclusion of the evidence that the psychic stimulus created must be such that the actor should have anticipated that he thereby created an unreasonable risk of injury to a person of normal constitution situated within his sphere of action, whose presence he knew or should have apprehended. In many of the nervous shock cases the alleged stimulus is patently inadequate to cause a response in a person of normal constitution.

In other cases the actor has simultaneously, by the negligent operation of a railway locomotive,[50] of a street car,[51] or in the handling of other dangerous instrumentalities, threatened the plaintiff with immediate bodily harm of a serious character, jeopardizing life or limb. The stimulus presented is patently adequate to create the strongest feelings of fright and other deep emotional disturbances in a normally constituted person.[52]

It is important to realize that practically always the stimulus can be analyzed in terms of its sufficiency or insufficiency to create a strong emotional reaction in an average person. This inquiry must always be taken into account in determining whether there has been such breach of duty in the creation of risk of injury as constitutes negligent dereliction.

A problem which has been considerably discussed by law writers and courts is how far the actor has a duty to bystanders, or to persons concealed in houses whose visual, auditory or tactile perception of a suddenly created stimulus engenders injurious fright. We think that since the right of any injured plaintiff to recover damages in the law of torts in cases of the negligence class, depends upon culpability, no recovery can be had by a person unless the defendant actor knew or should have known of his presence within the circle of risk at the time of creating or continuing an unreasonable, potentially harmful stimulus. It is believed that in practice the courts are following this limitation upon liability.[53]

Example a: Plaintiff may be outside the circle of risk because the defendant's stimulus does not come near enough to threaten any bodily harm to plaintiff.

Defendant railway company (D) built a switch from its main track at a point directly across the street from a house and lot owned by plaintiff (P), an

[50] As in Victorian Railways v. Coultas, supra, and Bell v. Great Northern Ry. Co., supra. See, also, the many cases against railroads cited in footnotes 7 and 8, supra.

[51] As in Kisiel v. Holyoke St. Ry. Co., 240 Mass. 29, 132 N.E. 622 (1921); Sundquist v. Madison Rys. Co., 197 Wis. 83, 221 N.W. 392 (1928) etc.

[52] Inadequacy of stimulus to produce the result in a person of average constitution was regarded as a proper ground for denying liability in the Scottish case of Cooper v. The Caledonian Railway Co., IV Session Cases (1902). Plaintiff alleged she suffered nervous shock from a carriage door swinging open and having its window broken. She was never for a moment in the smallest danger of injury. The trial judge reached this conclusion from the pleadings, without evidence and dismissed the case. The appeal court agreed that the stimulus, to be actionable, would need be one capable of producing an injurious response in an average person, but held evidence should have been received on this issue, and remanded the cause for hearing.

In Newton v. New York, N. H. and H. R. Co., 106 App. Div. 415, 94 N. Y. Supp. 825 (1905), X was commuting to New York on defendant's train when it negligently stopped in a tunnel with the result that a train following behind struck it. It was alleged that X suffered nervous shock which four months later caused him to die of acute dilatation of the heart. X's legal representatives, in an action against the RR recovered verdict and judgment for $12,500. Held, on appeal: Judgment reversed because there was no proof that the stimulus caused either physical injury or immediate nervous shock. The evidence showed that when the collision occurred, X was playing cards in a forward coach, and the tremor of impact was so minimal that X was merely moved forward slightly, not thrown against the seat ahead or onto the floor. The players continued at cards without their game board being thrown from their laps.

[53] The only exceptions seem to be occasional cases where courts have held an intentional wrongdoer liable for injury to one he could hardly have expected to be present.

adult female. Due to want of an adequate bumping post at the end of the track, D backed several cars over the end of the switch out into the street in the direction of P's house, but stopping 15 feet away from her yard. P alleged that she saw the spectacle from her house and suffered injurious fright in consequence, for which she sought to hold D in damages. The trial court sustained a demurrer to P's petition on the ground that the facts pleaded did not make out any legal cause of action. P appealed. Held: Affirmed, but, said the court, a right of action might have existed had D's cars rolled into P's yard thereby effecting a wrongful trespass.

Morse v. Chesapeake & Ohio Ry. Co., 117 Ky. 11, 77 S.W. 361 (1903).

Example b: Plaintiff may be outside the circle of risk because she is a detached spectator remote from the scene of action and so not within any duty of care owed by defendant as actor. In the field of ordinary negligence, we only hold the actor to abstain from creating unreasonable risks of injury to persons whose presence he knows or should apprehend.

(1) Plaintiff, while perfectly secure in her house, and not exposed to any personal peril, saw through her window the distressing spectacle of defendant's dog mangling her pet cat. Plaintiff sued defendant for negligently permitting his dog to escape custody and come onto her property, alleging that the episode caused shock and distress of mind leading to personal injury. P recovered verdict and judgment against D for $100 in the trial court.

Held, on appeal: Judgment reversed. In New York, under the rule of Mitchell v. Rochester Ry. Co., 151 N. Y. 107, 45 N.E. 354 (1896), a plaintiff who seeks to recover damages for negligently caused fright must prove a contemporaneous impact; here there was none and P was even far removed from the scene of action. P cannot recover damages. Buchanan v. Stout, 123 App. Div. 648, 108 N. Y. Supp. 38 (1908).

(2) In Nuckles v. Tennessee Electric Power Co., 155 Tenn. 611, 299 S.W. 775 (1927), plaintiff, while not in range of personal peril from the dangerous conduct, suffered shock and injury from seeing his son run over through D's negligence. Held: P could not recover damages. (Note carefully that Tennessee is one of the states which allows recovery for nervous shock without proof of contemporaneous impact.)

A further question has arisen as to whether the threat of injury which causes fright or emotional upset need be to the person of plaintiff, or one of his loved ones,[54] or whether it is sufficient if the plaintiff's apprehension is

[54] D, by negligent operation of his automobile, frightened P's mule so that it ran away. P was not in the buggy, but suffered great shock and consequent physical injury because of fright for her two children who were in the buggy. Held: P could recover damages from D. Spearman v. McCrary, 4 Ala. App. 473, 58 So. 927 (1912).

D negligently ran his truck into the basement of P's house. P suffered no impact, but because of fright for safety of his children who were in the basement, he sustained severe shock which led to a hysterical condition. Held: P could recover damages from D. Bowman v. Williams, 164 Md. 397, 165 A. 182 (1933).

On similar facts recovery was allowed for parental fright generated by apprehension of immediate bodily harm to children, in Hambrook v. Stokes Bros., 1 King's Bench (Eng.) 141; 94 L. J. K. B. 435 (1925), and in Cohn v. Ansonia Realty Co., 162 App. Div. 791, 148 N. Y. S. 39 (1914).

Courts in America have tended to put limits on liability in this series of cases by requiring the parent to be personally present within the circle of risk; if the parent suffers nervous shock as a mere spectator while situated outside the zone of peril, recovery of damages for nervous shock caused by defendant's conduct is denied. Waube v. Warrington,

for safety of his property whose immediate destruction is threatened by the defendant's conduct. The courts have reacted variously to this problem.[55]

B. Proximate Causation.

In times past there has been an unfortunate tendency in law to encrust concepts of actual or scientific causation with many metaphysical rules or principles. A leading example of this is the insistence of courts in many states that an act or omission cannot be the proximate cause of a particular event unless the result which actually happened was a "natural and probable" consequence. Such an idea is indeed foreign to realism, and as might be suspected, it is used by appeal courts as a mere device to enable them to deny existence of liability where it seems unconscionable or inequitable to make the defendant bear the risk of the particular loss of which the plaintiff complains. Actually what the courts mean when they use the above formula is one of two things:

1. The defendant cannot be connected with the transaction in a culpable relation if an average prudent man could not foresee the risk of injuring another by indulging such conduct. Analytically it would be better to bring

216 Wis. 603, 258 N.W. 497 (Mother, looking through window, saw daughter crossing street killed by D's negligence.)

Accord: Nuckles v. Tennessee Electric Power Co., 155 Tenn. 611, 299 S.W. 775 (1925).

In Hambrook v. Stokes, supra, the English courts allowed a parent to recover damages for nervous shock caused by apprehension that a child on the way to school had been injured by a runaway lorry which rolled down a long hill when the driver negligently left it without the brakes set. The parent here was not in peril of personal harm, and the decision has been criticized as extending liability too far. It may be argued on facts of the case that the presence of the parent in the vicinity was known or could be anticipated and that a parental fright reaction was foreseeable.

If the parent is entirely absent from the scene of action, and reacts only as the result of an after report, the risk of injury seems too remote to be chargeable against the actor.

[55] Most courts, to draw limits of liability in the "nervous shock" cases consonant with their views of policy, have made it an arbitrary requirement that the fear be for self or family and not for property. See Waube v. Warrington, 216 Wis. 603, 608, 258 N.W 497, 499 (1935); Dulieu v. White & Sons, (1901) 2 K.B. 669.

In a recent Nebraska case, however, the court declined to impose such limitations on liability and permitted recovery of damages where nervous shock was engendered by concern over a dairy herd poisoned by bran negligently sold by D to a dairyman, X.

The facts were quite interesting. D, a farmer, having forgotten that he had put arsenic in bran for the purpose of poisoning grasshoppers, sold the bran to X. X fed the bran to his cows and the next morning milked them and made deliveries to customers. Late in the forenoon five cows died and five others were made sick. X allegedly suffered severe nervous shock from injury to his herd and fear that he would lose his dairy business, and from apprehension that customers, whom he promptly notified, might suffer arsenious poisoning. X was unable to work after this episode, due to impaired health, and died nine months later of a decompensated heart. There was medical testimony that this was caused by an excessive emotional disturbance. (Note great danger of imposition: Could death from cardiac decompensation be scientifically attributed to nervous shock as cause, particularly in face of a nine month interval between stimulus and alleged response?!)

X's widow sued D for negligently causing death of her husband and injury to the dairy business. The Supreme Court of Nebraska upheld a recovery for both items, by a five to two decision. Rasmussen v. Benson, 133 Neb. 449, 280 N.W. 890 (1938).

It is doubtful whether many American courts will permit recovery for injury due to fright or shock engendered by a negligent act which threatens harm only to another's property, unless the conduct also carries a foreseeable risk of personal injury. Serious doubts must also be voiced, from a scientific point of view, about existence of any actual cause-effect relationship in the Rasmussen case between emotional upset and cardiac decompensation nine months later.

in this type of consideration under the heading of dereliction, and to say that lack of foreseeability of any harm prevents the conduct from being negligent. Probably the courts have not done this because it has been traditional practice to submit the question of negligence to the jury, and a jury finding on conflicting evidence is final. The question of causation also is submitted to the jury, but the appeal courts have developed the practice of overthrowing the verdict and reversing the judgment, if in their opinion the result was not "a natural and probable consequence of the defendant's act." This enables the court to refuse liability despite the jury verdict, in cases where it thinks public policy is opposed to undue extension of liability.

2. The court may mean in holding that the injury complained of is not the "natural and probable consequence" of the defendant's act, that the whole injury, in type, was so bizarre and unusual as to be a remote possibility in the expectation of any reasonably prudent actor. This, too, could be referred analytically to the duty-dereliction terms and made a circumstance tending to prove that there was no negligence. It could even more accurately be considered under the term "damages," and liability excluded on the ground of remoteness, which technic would merely indicate the appeal court's opinion that public policy was opposed to extending liability so far.

The reader will see that courts in the main are concerned with using devices for placing the risk of loss or injury equitably as between actor and person acted upon in a given species of case. It is not surprising that the courts use all four terms of the liability formula (duty $\rightleftarrows$ dereliction $\rightleftarrows$ proximate causation $\rightleftarrows$ injury) like keys of a piano board.

In the nervous shock cases some appeal courts have weeded out the more extreme, bizarre cases and denied liability, on the ground that the nervous shock or injury was not the "natural and probable consequence" of the defendant's conduct, so that there was a failure of causation.[56]

We think it would be much better, however, to keep the term "proximate causation" as simple as possible and to use it in the sense of "actual causation." This would conform legal practice to scientific truth, and clear away much confusion that has arisen in times past from loose and varied usage of the concept of causation in the liability formula.

Heretofore we have considered the mechanisms involved in psychic stimulation and the effects and diseases which might be engendered thereby. It will be necessary in time to explore further by adequate scientific studies

[56] Mitchell v. Rochester Railway Co., 151 N. Y. 107, 45 N.E. 354 (1896). (One ground for denying recovery for abortion allegedly caused by fright without impact, when D's horses were negligently permitted to all but run down plaintiff in the street. Two other grounds were given for refusing a right of action: (1) policy argument: difficulties of proof and likely encouragement of fictitious suits; (2) since there can be no recovery for fright negligently caused, there can be no recovery for physical consequences of fright. This last deduction has been widely attacked as specious.)

Miller v. Baltimore and Ohio RR. Co., 78 Ohio St. 309, 85 N.E. 499 (1908). (As in Mitchell case, supra, one ground for denying recovery for injury due to fright, negligently caused, but without contemporaneous impact.)

the relationship of psychic stimulation to all the diagnosable disease entities and syndromes.

At this time we should like to lay down certain orientating principles which might be useful in appraising particular medico-legal claims:

(1) In the usual tort case, the injury claimed by the plaintiff is attributed to a *single* frightening stimulus of fairly short duration. Cases of repeated exposure to the fear-producing stimulus negligently created by defendant arise only rarely, such as continued blasting operations over a period of weeks or months, where large stones continue to be thrown on the roof of plaintiff's dwelling.[57]

The physician must consider whether a causal connection can be postulated between the single stimulus of described severity and the alleged consequential injury or disease. In more than one case which has come before the courts in the past, the plaintiff has had a silent interval with no substantial symptoms, lasting for days, weeks or months separating stimulus and alleged response.[58] Knowing as we do that the immediate physiological changes engendered by fright tend to subside and pass away fairly quickly when the efficient stimulus is removed, long silent periods with no "bridging symptoms" must be looked upon with grave doubts when an effort is later made to establish a causal connection. The bridging symptoms may consist of immediate prostration with various symptoms, such as immediate and persistent pain, or of radical alterations in the behavior pattern, as we find in the so-called traumatic neuroses.

[57] Green v. T. A. Shoemaker & Co., 111 Md. 69, 73 Atl. 688 (1909), 23 L. R. A. (N. S.) 667.

[58] A good example is the New York case of Hack v. Dady, 134 App. Div. 253, 118 N. Y. Supp. 25 (1909). Plaintiff, a pregnant woman, was walking along a city street with her two children when negligence of defendant in laying a main caused an explosion in a pot of molten lead. A few drops of the molten lead were cast upon P's hand and clothes, but she quickly flicked them off and suffered only a small superficial burn. P sued D, claiming that fright and nervous shock caused a miscarriage to occur three and a half weeks after the accident, a second miscarriage six months thereafter terminating a two months' pregnancy, and a third miscarriage three months after the second terminating a three months' pregnancy. On the first trial, Dr. A testified positively that these injuries were due to psychic reactions engendered by fright. P recovered verdict and judgment in the trial court, but this was reversed on appeal on the ground that the New York requirement of impact as a prerequisite to recovery for nervous shock, is not satisfied unless the impact contributes substantially to production of the nervous shock or the final injury (miscarriage).

On a second trial, P called Dr. B instead of A. B testified positively that the miscarriages were due to physical injury caused by the spark landing on P's hand. P recovered verdict and judgment for $2000, and on appeal this was affirmed.

This case illustrates the imposition which may occur in this species of litigation. It is characteristic of a large group of cases where:

(1) The minimal trauma was too slight to produce a miscarriage.
(2) The trauma was to a remote part of the body rather than to the abdomen.
(3) There was not a sufficient frightening stimulus to prove psychic miscarriage.
(4) The long time interval of three and one half weeks without proof of bridging symptoms speaks almost conclusively against causal relationships of either trauma or psychic influences.
(5) The history of the case strongly suggests that the repeated miscarriages were due to some independent cause unrelated to D's negligence.

There is a notable exception to the expectation of immediate reaction. It has been observed that when men are under sudden and great emotional stress, as in shipwreck, the final reaction is delayed, oftentimes until after the person so exposed has been put ashore and has gone inland. The inference to be drawn from this phenomenon is that "time for deliberation or contemplation" must be allowed for in reckoning what the final total reaction will be. If the person has gone far beyond such period without appearance of any symptoms, and at a later date claims a disability from his frightening experience, it is proper, unless there be very exceptional proof, to deny the causal connection.

(2) The test of injury is not a mere transient invasion of mental tranquillity speedily passing away, but whether or not we can say scientifically that the stimulus produced some disability in the form of temporary or permanent or partial or total incapacity for continuing usual pursuits. Needless to say, pain and the like are compensable as separate items, in addition to any physical injury and loss of time from work.

(3) If the plaintiff be subjected to some frightening stimulus which causes no injurious effect or disease, but after a substantial interval of time he begins brooding over what might have happened and thus becomes disabled by neurosis, this is held by the law not to be compensable.[59] It is believed that this view is sound, because when the interval is so long, independent factors may be operative. Though there may be actual causation in a particular case, it is defensible for the law to find a failure of causation on grounds of policy and the conjectural character of the evidence.

(4) *Proof of malingering.* Malingering may have two different legal effects, namely:

a. If the claimant has suffered no injury at all and his claim is a pure fabrication, proof of this, if credited by the trier of fact (the jury, or the judge if there be no jury) defeats the right to recover *any* damages, by disproving existence of the terms *causation* and *injury* of the liability formula.

b. If the plaintiff has suffered some genuine injury, but is malingering

[59] Swift & Co. v. Ware (Ga. Appeal), 186 S.E. 452 (1936).

Phelps Dodge Corporation v. Industrial Commission, 46 Ariz. 162, 49 P. (2d) 391 (1935). X, a miner, ran 500 feet to reach fresh air after blast of a "missed hole" caused shafts and drifts of the sulphide ore mine to become filled up with smoke, gas and dust. He suffered no injury but thereafter developed a neurosis from brooding over what might have happened to him, and in that event what would have been the lot of his family. Held: Since the neurosis was not caused by nervous shock produced by the episode, but by subsequent brooding, the neurosis was not result of an "*injury*" sustained by accidental means, and was not compensable under terms of the Arizona Compensation Act.

In certain interesting cases claim has been made under Workmen's Compensation Acts for suicide due to insanity allegedly caused by an accidental injury received in course of employment. Courts have held it is not enough that insanity was indirectly caused by the injury if the more immediate cause was worrying and fear of losing employment (Grime v. Fletcher [Eng. 1915], 1 King's Bench 734; 8 B. W. C. C. 11, C. A.) or depression and brooding over inability to work. (Withers v. London, Brighton and South Coast Rail Co. [Eng. 1916], 2 King's Bench 772, 9 B. W. C. C. 616, C. A.)

There may be *actual causation* here, but it must be admitted that lapse of time, the entry of independent causes, and difficulties of proof, justify the law in drawing an outer line of liability, though somewhat arbitrarily, in this type of case.

as to the extent of symptoms or duration of disability, proof of these facts will not destroy the cause of action, but will only operate under the term "injury" in the trial formula to reduce the amount of damages recoverable.

Probably malingering of the first type is rather rare. It is rather dangerous in point of trial strategy for defendant to try to prove malingering, unless he can set his contention up with considerable strength. To create a mere suspicion of malingering usually acts as a boomerang, for one needs to impute a fraudulent intent to the plaintiff, and a jury deeply resents the making of such charges without strong proof. These considerations account partially for the infrequency with which lawyers raise malingering as a defense in the nervous shock cases.

We feel it necessary, however, to make some allusion to malingering, and we do so under two headings, namely:

a. Proof of malingering by lay investigation and testimony. Insurance company adjusters, claim agents, or specially retained detectives are often able to observe the claimant when he is acting spontaneously and completely unaware that he is being watched. A person who claims to be paralyzed may walk; one who uses crutches may cast them aside; one who is kept constantly in bed in a state of prostration may be seen vigorously cleaning house; various neurological symptoms may disappear. Sometimes it is possible for the observer to take motion pictures, and the courts have held that these may be shown in evidence. Obviously lay evidence of this variety depends upon producting a flat contradiction so that the claimant is made out a complete liar.

b. Medical proof of malingering. The doctor must apply his common sense as a layman, as well as his special medical talents. In many cases it will be found that the case falls in class b, where there is some genuine disability which the patient is exaggerating, oftentimes by the process known as "unconscious" malingering. Usually a more just result can be reached by considering such factors as evidence of preëxisting impairment of personality, under the term "injury" of the trial formula, and discounting the amount of damages accordingly which one would attribute to the accident itself.

It is held that a doctor who has examined a claimant is entitled to give his opinion that he is a malingerer,[60] and that even without benefit of such examination he may give his opinion after observing the claimant on the witness stand.[61]

Hysteria and malingering. Distinguishing hysteria and malingering is one of the recurrent problems, and so we single it out for special attention.

Hysteria, using the word in the narrow and technical diagnostic sense,[62] is a disorder associated with childish behavior. Not only is the behavior

[60] Klein v. Medical Building Realty Co. (La. App.), 147 So. 122 (1933).
[61] St. Louis, I. M. & S. R. R. v. Osborne, 95 Ark. 310, 120 S.W. 537 (1910).
[62] LINDEMANN, E.: Hysteria as a problem in a general hospital, Med. Clin. North Am., 1938, xxii, 591.

childish, but the patient often looks younger than her years and may have a childish build and under-developed organs. The typical cases have symptoms that are almost naïve in their obviousness: a bride loses her eyesight when her husband is ordered to sea duty; a boy has "fits" when his father and mother quarrel; a young married woman who does not want any more children develops spastic adduction of the legs. These patients show such symptoms with *"belle indifference";* they do not worry about the symptoms. They do not, however, see the connection between the situation they are in and the symptoms. The primitive, childlike idea "I can't stand it, so I'll be sick and get out of it" was probably in their heads, but they discarded it, acted on it and forgot it. This is the mechanism known as conversion with amnesia. The childish and unworthy thought is converted into action, the unbearable situation is converted into protective invalidism. The amnesia is childish in its simplicity and completeness. Under hypnosis and by associations such mechanisms can sometimes be brought to light; explanation often cures. If not, a shrewd "putting of the shoe on the other foot" by the physician causes the symptom to disappear.

Such in a simplified schematization is the mechanism of hysteria. Why is it not malingering? Where is the line? Can it be drawn?

Malingering is willful and conscious falsification. Symptoms are imitated with an ulterior motive. The simple cases, such as men who escape army duty by eating soap, are easy enough to understand. But others are not so simple. For example, a woman slipped on some garbage on the stairs of a railroad station; falling, she fractured her coccyx and was taken to a hospital. Here roentgenograms showed the injury. In a few days she returned home well. Here she was apparently happy until a lawyer asked her a lot of questions and suggested to her the possibility of getting damages from the railroad. She returned to the hospital in a wheel chair, said her legs were weak and painful and talked about law suits. The diagnosis this time was "malingerer" and a mental test showed her to be a moron (mental age about nine years). She was sent home. Six months later she returned to the hospital with stiff, weak legs and anesthesia up to the thighs. The examiner could put pins into the skin and muscle without hurting her. The muscles showed atrophy from disuse. This time the diagnosis was "hysteria." In her moronic mind she had made the conversion and forgotten it. Starting as a rather stupid malingerer she had become an automatic hysteric.

It is obvious that a line cannot be drawn in some cases. Many cases of hysteria start with more or less conscious wishes for a symptom to gain an end. Some malingerers are so obvious and simple that they are to be classed as feeble-minded, others are smart but deceitful to such a degree that they are psychopathic. A few are just average folks who are trying out an acted lie. The differential diagnosis takes a man not only with psychiatric experience, but shrewdness. Each case must be studied thoroughly and individually.

C. The term "injury" in the trial formula and pertinent doctrines of the law of damages.

If the defendant was guilty of a willful, intentional invasion of plaintiff's rights of personality, as for instance committing an "assault" by creating an immediate apprehension in plaintiff of immediate bodily harm, this gives a technical cause of action for some damages, even though no actual harm was suffered.[63]

Very few of the nervous shock cases fall in this category, but depend on allegations of negligence, and such cases cannot be maintained in court without proof of actual injury or damages. The plaintiff is entitled to recover for physical and mental pain and suffering past and future, for any physical injury itself, for medical expense, and for loss of earnings.

It is characteristic of the many "nervous shock" cases that the response to the particular stimulus is quite excessive, more than that which a person of average constitution would give. The stimulus may be the mere occasion or circumstantial cause of the response when preëxisting factors constitute the substantial cause. In science we are accustomed to sorting out all the contributing causes and allotting a just share of responsibility to each factor. The law has developed on a cruder basis, not apportioning causation as such, but holding that an actor is or is not a substantial cause of the injury; if so, he is liable for the whole injury, if not, he is legally responsible for none of it. In the main, this "all or none" way of treating causation does not work great injustice, but it falls down when a $100 impact produces a $10,000 injury because of idiosyncrasy of the plaintiff. What can be done to rectify this situation, is a major problem discussed elsewhere.[64] For one thing, a defendant must be alert to prove that the disability in large part represents a preëxisting impairment, for which the plaintiff cannot recover damages, rather than mere excessive injury due to the accident itself operating on a vulnerable person. In the latter case, American courts allow full compensation because of their refusal to apportion causation.[65]

[63] Usually it is said the actor must have the apparent means of "then and there" converting threat into injury; hence, it is necessary that the actor be close at hand, and a threat made at a distance, by telephone, would not be sufficient to constitute an "assault." If injurious fright were caused by such a "long distance" threat, the right to hold the speaker in damages might well turn on these questions:

(1) Did A, in speaking, maliciously intend to cause B harm through fright? If so, A should be held liable in damages.

(2) If the answer to (1) is "no," A's right to recover damages must depend on proof of negligence:

a. Did A know that B was idiosyncratic or excessively vulnerable and so apt to be caused injurious fright by the threatening language? If so, A should be held liable in damages.

b. If A did not know of any idiosyncrasy, should he have foreseen that his verbal conduct would be likely to cause injurious fright in a listener of average constitution? If so, A should be held liable in damages.

[64] See SMITH, H. W., and SOLOMON, H. C.: Traumatic neuroses in Court, in Smith on Scientific Proof and Relations of Law and Medicine, Matthew Bender & Co., Albany, N. Y. (In press).

[65] See, for instance, Flood v. Smith, 126 Conn. 644, 13 A (2d) 677 (1940). As the result of an automobile collision caused by negligence of D, P_1 and P_2 sustained injuries in excess

On the other hand, there is now respectable authority, which is doubtless destined to become the universal rule, that where medical testimony can separate out that part of the injury due to the accident, and that part due to preëxisting causes or idiosyncrasies, the plaintiff can recover damages only for the first.[66] As we have said, the case may be otherwise where the actor knows or should know of the other person's preëxisting disease or idiosyncrasy,[67] for here the duty of due care may be held to require more cau-

of those which an average person would have suffered from a like stimulus. Proof showed that P_1, a 28 year old man, two years previously had been injured in another automobile accident, suffering a fracture of his skull and impairment of his nervous system, but with substantial interim recovery. P_2, his companion, was a 70 year old library cataloguer, who previous to the accident, had suffered two nervous breakdowns and had undergone surgery for the removal of a cancerous breast. Both P_1 and P_2 were bruised in the accident and suffered extreme nervous shock, in P_2's case aggravated by her morbid fears that a bruise on the site of the amputated breast would reactivate her cancer. The jury awarded P_1 $3500 and P_2 $4100. The trial court thought these damages excessive and granted D's motion to set aside the verdict and order a new trial unless P_1, by remittitur, relinquished $1275 of the verdict, and P_2 $2027. P_1 and P_2 appealed.

Held: The damages awarded by the jury were not excessive. Cases remanded with orders for trial court to enter judgment for the full verdicts.

The Connecticut Supreme Court said: "The plaintiffs are entitled to recover full compensation for all damage proximately resulting from the defendant's negligence, even though their injuries are more serious than they would otherwise have been because of preëxisting physical or nervous conditions."

It is submitted that the result of this case is wrong, for it imposes a liability for a total end result only partly caused by the defendant's stimulus.

[66] Moore v. Tremelling (U. S. Circuit Court of Appeals, Idaho), 78 F. (2d) 821 (1935); same case, on later appeal, 100 F. (2d) 39 (1938).

X fractured his leg and retained surgeon Y to treat it. As a result of negligent failure to take post-reduction roentgenograms at intervals after properly setting the fracture, Y failed to discover that the bones had slipped out of apposition. X developed a bad end result. Held: X could recover compensatory damages from Y for the result of his malpractice but not for such part of the end result as would have been due to the original fracture properly treated. The burden was on X to separate out the two items of damage.

In certain recent Workmen's Compensation cases, it has been held that in assessing damages, causation should be apportioned between accident and preëxisting factors: Ashland Limestone Co. v. Wright, 219 Ky. 691, 294 S.W. 159 (1932).

The same result has been reached by reducing the percentage of total disability which would be allowed if the accident were the sole cause: Moray v. Industrial Commission of Utah, 58 Utah 404, 199 P. 1023 (1921); Sykes v. Republic Coal Co., 94 Mont. 239, 22 P. (2d) 157 (1933).

This meticulous apportionment between accident and preëxisting causes is a new trend which is more scientific and equitable than the practice of holding a merely negligent actor fully responsible for injury only partially caused by him.

[67] Defendant Wing was indicted for maliciously discharging a gun, whereby a woman, named M. A. Gifford, was thrown into convulsions and cramps.

Defendant had discharged the gun in a highway, for the purpose of killing a wild goose, at a place not more than two or three rods from the house in which Miss Gifford lived. He asserted that it was his right to fire the gun as he pleased, for the reason that the shooting occurred on a neck of land to which citizens had resorted since time immemorial for the purpose of fowling.

Evidence on the trial proved that Miss Gifford had been severely affected with a nervous disorder for some six years, with the result that she was uniformly thrown into a fit upon hearing a gun, thunder, or any other sudden noise, or by hearing the words *gun, ammunition,* etc., mentioned. It was shown that defendant was warned of this fact and requested not to fire the gun, but that he did so nevertheless.

"The [trial] judge instructed the jury, that if they believed that the defendant knew, or had good reason to believe, that the consequences above mentioned would be produced by the firing of the gun, and had notice to that effect immediately before the firing, they should return a verdict of guilty; which they did accordingly. If this instruction was wrong, a new trial was to be granted."

Held, on appeal: Conviction affirmed. Chief Justice Parker of the Supreme Judicial Court of Massachusetts said:

tion. The courts are less likely to sort out damages where the actor is guilty of an intentional battery or other wrongful invasion of the plaintiff's rights of personality. But the result here is best explained on the ground that the actor is a thorough-going culprit, worthy of having punitive damages assessed against him by way of example, so that the court feels no deep concern about apportioning damages with scientific delicacy in his behalf, or weighing out justice on golden scales, as it were.

The physician should go to court carefully prepared by study of the pretraumatic personality of the claimant, and thorough neurological and psychiatric examinations, and a due regard to the nature and adequacy of the stimulus, the immediacy of symptoms and the nature and continuity of disability, to say what portion of the total injury or damages should be allocated to the accident and what part to preëxisting factors. The physician should be very firm in this respect, for the law in many states is now in such condition that this vital distinction is blurred, and grossly excessive verdicts are being entered against defendants for injuries which they only partially caused. It is our opinion that a competent examiner can arrive at a satisfactory estimate in making this apportionment, but that he must individualize each case.

Conclusion

We have endeavored in this communication to make certain salient points, as follows:

(1) A study of the nervous shock decisions demonstrates the absence in times past of any adequate criteria for judging actual causation of the alleged injury or disease by the given stimulus.

(2) We saw that the chief stimulus which underlies the nervous shock cases is fright, and the chief disabilities claimed are "nervous shock" with consequential disability, usually temporary; traumatic neuroses; and alleged psychic abortions or miscarriages.

(3) We have given an account of the current concept of "nervous shock," showing in general the mechanism of its production.

(4) We have mentioned those independent diseases, aside from the various neuroses and immediate injuries, for which there is now substantial

". . . we think the offence described is a misdemeanor, and not a nuisance. It was a wanton act of mischief, necessarily injurious to the person aggrieved, after full notice of the consequences, and a request to desist. The jury have found that the act was maliciously done.

"In the case of Cole v. Fisher, 11 Mass. R. 137, Chief Justice Sewall, in delivering the opinion of the Court, speaking of the discharging of guns unnecessarily, says, if it is a matter of idle sport and negligence, and still more when the act is accompanied with purposes of wanton or deliberate mischief, the guilty party is liable, not only in a civil action, but as an offender against the public peace and security, is liable to be indicted, &c.

"Now the facts proved in the case, namely, the defendant's previous knowledge that the woman was so affected by the report of a gun, as to be thrown into fits, the knowledge he had that she was within hearing, the earnest request made to him not to discharge his gun, show such a disregard to the safety and even the life of the afflicted party, as makes the firing a wanton and deliberate act of mischief."

Commonwealth v. Wing (Supreme Judicial Ct. of Mass.), 9 Pick. 1, 19 Am. Dec. 347 (1829).

medical evidence that psychic stimulation may be a causal factor in pathogenesis.

(5) We have stressed the need for continued and systematic study of the relations of all disease states and syndromes to determine what effect psychic stimuli, particularly of sudden and severe character, may have either on production of the condition or upon its activation, aggravation, or acceleration.

(6) We have pointed out that the idiosyncratic or excessively vulnerable person, for reasons of social policy, should not be granted more legal protection against mere negligence of an inadvertent actor, than the person of average constitution receives.

(7) The fact last mentioned, coupled with the recognized fact that emotional stimuli may be mere trigger mechanisms to cause appearance of symptoms of a preëxisting disorder, requires the most careful apportionment of final injury between accident and preëxisting impairment or disease of the subject.

(8) We have endeavored to provide a rationale, both legal and scientific, for study of the existence and extent of liability in the nervous shock cases, sometimes referred to generically as cases of "liability without impact." Here we stress the necessity for remembering the essential terms Duty + Dereliction + Proximate Causation + Injury, whose concurrent existence must be proved by a preponderance of substantial evidence before a plaintiff can establish any right of action.

(9) It is emphasized that with the advance of scientific knowledge, especially in physics, "physical impact" in the sense of striking the person of the plaintiff with a "physical object" becomes meaningless. Waves of air from an explosion may cause "blast injury" or traumatic sounds. Waves of ether may cause visual injury or burns. These involve "physical contact" just as truly as striking the plaintiff with a weapon. By the same token the distinction between "organic" and "functional" disorders has been eliminated. Disorder of function in an organ cannot occur without structural changes in that organ, although these may be temporary. If the law momentarily clings to distinctions between gross and microscopic injury and false distinctions between "organic" and "functional" disorders, it can be justified only by difficulties of proof. This justification should vanish with introduction of proper criteria of proof and of improved mechanisms of trial for handling scientific issues.

(10) We call special attention to the need for studying the stimulus and its adequacy to produce a response in a person of average constitution, as this consideration must be taken into account in determining to what extent the response of the particular patient is due to his idiosyncrasy, excessive vulnerability or preëxisting impairment.

INTRACRANIAL ANEURYSMS—A REPORT OF THIRTY-SIX CASES*

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FROM November 1935 to April 1942, there were observed in the laboratories of the Queens General Hospital 36 cases of intracranial aneurysm affecting the cerebral arteries in a total of 3080 autopsies. The report that follows will describe the pertinent anatomical and some of the clinical features associated with these aneurysms. On the basis of the histopathological findings, an attempt will be made to throw further light on the mechanism of rupture of the so-called "berry" aneurysms.

Numerous excellent descriptions of the clinical syndrome and of particular pathological features of ruptured aneurysms of the cerebral arteries abound in the literature. In a study of cerebral aneurysms by Richardson and Hyland,[1] references will be found to most of the earlier studies. Forbus [2] first showed the frequent association of medial defects in the cerebral arteries and the congenital type of aneurysm. He found the defects at the bifurcation of the cerebral arteries in cases with and without aneurysms. Forbus postulated as the cause of the aneurysms, a congenital defect of the muscular tissue of the media which when exposed to intra-arterial pressure, lead to aneurysmal dilatation and sometimes rupture. Glynn [3] in a study of routine sections of the cerebral arteries in cases with and without aneurysms, found medial defects in 80 per cent of both groups. By means of injection experiments, he found no weakness or bulging at the site of naturally occurring or experimentally produced defects. The latter were produced by sectioning the adventitia and media of the artery and leaving the intima intact. Since the elastica is entirely confined to the intima of the cerebral arteries, he concluded that the weakness of the vessel wall is entirely a function of the state of the elastic tissue. He contended that dire consequences result when atheroma affects the cerebral vessels with consequent destruction of the elastica. He held that medial defects play no part in aneurysm formation. Richardson and Hyland believe that "the medial defects are probably developmental and play a part in causing aneurysms, but that there is another unrecognized acquired lesion which causes degeneration of elastic tissue." In a complete study of 40 cases with intracranial aneurysms, they reported 27 cases with rupture, and 13 cases of unruptured aneurysms. Altogether 53 aneurysms were found in their 40 cases, of which two were arteriosclerotic and the remainder of the congenital "berry" type. They reported an unusually high incidence of intracerebral hemorrhage in their series, describing

* Received for publication August 11, 1942.
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19 instances of this complication associated with a varying degree of subarachnoid hemorrhage. Ten of the 19 hemorrhages were located in the frontal lobe, whereas the remaining nine were found in the temporal lobe. The two authors recorded no instances of mycotic or syphilitic aneurysm. Of the latter, the statement is made that "syphilis plays little or no part in the formation of cerebral aneurysms." Concerning mycotic aneurysms, they refer to Turnbull's study, in which 15 of 44 aneurysms were of the mycotic variety. Martland,[4] in a study of fatal spontaneous subarachnoid hemor-

CHART I

Résumé of 36 Cases of Intracranial Aneurysm

Case No.	Age	Sex	Type of Aneurysm	Cause of Death	Duration of life	Remarks
1.	45	M	Berry	Bilateral frontal lobe hemorrhage	Six weeks	Double ruptured "berry" aneurysms of anterior cerebral arteries.
2.	12	M	Berry	Intraventricular hemorrhage	One week	History of falling off bicycle, preceded by dizziness.
3.	46	F	Berry	Subarachnoid hemorrhage	Found dead	Necrosis of wall of aneurysm with polynuclear inflammatory reaction. Polycystic kidneys, cysts of liver; hypertension for many years.
4.	65	F	Arteriosclerotic	Subarachnoid hemorrhage	Found dead	
5.	56	F	Arteriosclerotic	Subarachnoid hemorrhage	Found dead	Large aneurysm measuring 4 cm. in diameter found deep in temporal lobe.
6.	33	M	Mycotic	*Staph. aureus hem.* sepsis	Incidental finding	Medusa-head minute aneurysm of leptomeningeal artery; cavernous sinus thrombosis.
7.	44	F	Syphilitic	Subarachnoid hemorrhage	Found dead	Miliary gummata of kidney; active syphilitic hepatitis with cirrhosis.
8.	42	F	Berry	Subarachnoid hemorrhage	Two days	Blood pressure, 236 mm. Hg systolic and 110 mm. diastolic; hypertrophied heart.
9.	27	F	Mycotic	Intraventricular hemorrhage	More than four hours	*Strep. viridans* subacute bacterial endocarditis.
10.	43	M	Traumatic	Cerebral hemorrhage	Ten days	Trauma to head one month previously; aneurysm connecting internal carotid artery and cavernous sinus.
11.	18	F	Mycotic	Cerebral hemorrhage	? (no definite symptoms)	Picture of cerebral hemorrhage masked by debility associated with *Strep. viridans* subacute bacterial endocarditis.
12.	43	M	Berry	Subarachnoid hemorrhage	Five days	No previous episodes; onset with headache, convulsions.
13.	14 mos.	F	Mycotic	Meningitis	Incidental findings	Influenzal meningitis.
14.	69	F	Berry	Encephalomalacia	Incidental findings	Marked cerebral arteriosclerosis in vessels other than aneurysm.
15.	51	M	Mycotic	*Staph. aureus hemolyticus* sepsis	Incidental findings	Multiple kidney abscesses; multiple small aneurysms of subcortical vessels.
16.	17	F	Mycotic	*Staph. aureus hemolyticus* sepsis	Incidental findings	Multiple kidney abscesses; multiple small aneurysms of subcortical vessels.

CHART I—*Continued*

Case No.	Age	Sex	Type of Aneurysm	Cause of Death	Duration of life	Remarks
17.	73	M	Arterio-sclerotic	Subarachnoid hemorrhage	Five days	Blood pressure 180/100; hypertrophied heart; marked generalized and cerebral arteriosclerosis.
18.	31	M	Berry	Subarachnoid hemorrhage	Three days	Active sickle cell anemia.
19.	57	F	Berry	Cerebral hemorrhage	Incidental findings	Blood pressure 200/140; syndrome unrelated to aneurysm.
20.	58	F	Arterio-sclerotic	Subarachnoid hemorrhage	Four days	Monckeberg's sclerosis of intracavernous portion of internal carotid artery.
21.	14	F	Mycotic	Cerebral hemorrhage	Seven days	*Strep. viridans* subacute bacterial endocarditis.
22.	58	F	Arterio-sclerotic	Subarachnoid hemorrhage	Six hours	Marked generalized arteriosclerosis.
23.	28	F	Syphilitic	Subarachnoid hemorrhage	28 hours	One previous episode; positive blood Wassermann; active meningo-vascular syphilis.
24.	61	F	Arterio-sclerotic	Subarachnoid hemorrhage	18 hours	Moderate cerebral arteriosclerosis.
25.	16	F	Mycotic	Subarachnoid hemorrhage	24 hours	*Strep. viridans* subacute bacterial endocarditis.
26.	45	F	Arterio-sclerotic	Cerebral hemorrhage	Six hours	Unilateral frontal lobe hemorrhage; moderate cerebral arteriosclerosis.
27.	46	M	Berry	Subarachnoid hemorrhage	Found dead	History of hypertension.
28.	48	F	Berry	Traumatic shock	Incidental finding	——
29.	56	M	Berry	Subarachnoid hemorrhage	24 hours	Hypertrophied heart.
30.	25	F	Berry	Subarachnoid hemorrhage	Found dead	Small amount of thymic tissue, hypoplastic aorta and adrenal.
31.	50	F	Berry	Subarachnoid hemorrhage	Found dead	——
32.	11	F	Mycotic	Subacute bacterial endocarditis	Incidental finding	Two aneurysms of convexity of parietal and occipital lobes.
33.	29	F	Berry	Subarachnoid hemorrhage	More than four hours	Red headed; enlarged thymus, hypoplastic aorta and cerebral vessels.
34.	35	F	Berry	Subarachnoid hemorrhage	10 minutes	Found dead at home 10 minutes after notification of father's death.
35.	52	F	Arterio-sclerotic	Subarachnoid hemorrhage	Found dead	Paget's disease of skull; fracture of skull.
36.	16	F	Mycotic	Cerebral hemorrhage	More than 24 hours	*Strep. viridans* subacute bacterial endocarditis.

rhage in Medical Examiner's material, reported 38 berry aneurysms in a total of 49 cerebral aneurysms. He stressed the fact that fully 2 per cent of sudden natural deaths are due to ruptured aneurysms. Of the 54 cases, 21 were either found dead or died within 30 minutes of collapse, and 41 were dead within 12 hours of the onset of the initial symptoms. Dial and Maurer [5] described seven arteriosclerotic and two syphilitic aneurysms in a series of 13 cases of subarachnoid hemorrhage. In a special article, McDonald and Korb [9] presented the most extensive bibliography and analytical study of 572 cases, with 49.5 per cent arteriosclerotic, 12.2 per cent embolic or mycotic, and only 5.6 per cent syphilitic, with 32.7 per cent listed as normal, the latter ostensibly of the "berry" type.

Material. The cases included in this study represent those encountered in the routine autopsy service of a general hospital laboratory, and a group of cases performed under the direction of the Medical Examiner's office in the County of Queens. Only those cases in which a definite aneurysm or site of rupture was identified are described. Excluded from the reported series are the cases of fatal subarachnoid hemorrhage in which the site of bleeding was not identified; and uniform aneurysmal dilatation of the cerebral arteries demonstrating no discrete aneurysmal sac. Chart 1 lists the material studied, with some of the pertinent clinical and pathological data.

Age and Sex. There were 28 females and 10 males in the series. The ages ranged from 14 months to 69 years, with a mean age of 40 years.

Clinical Features. Of the 36 cases encountered, no previous clinical data are available in 20. Eight of these are represented by incidental findings at autopsy, whereas the remaining 12 were found dead or died before admission to the hospital. Chart 2 outlines the duration of life after onset of symptoms in the 28 cases in which this information was present.

CHART II

Duration of Life after Onset of Symptoms in 28 Cases

Found dead	Less than 1 hour	Less than 12 hours	1 day	2 days	3 days	4 days	5 days	6 days	More than 1 week
12	0	4	4	2	1	2	2	0	1

Coma was noted as the presenting symptom in 10 of the 16 cases observed on the wards of the Queens General Hospital. Severe headache was noted as a prominent symptom in five instances; convulsions were seen on four occasions. Less frequent symptoms were stiff neck (3), hemiplegia (2), and dizziness, vomiting, diplopia, and a buzzing sound in the head. The latter was noted in the single instance of traumatic arteriovenous aneurysm of the internal carotid artery and the cavernous sinus.

Of significance was the presence of hypertension in nine cases. Case 34 is of particular interest in demonstrating the influence of emotional upset in the production of hypertension, and its relation to the rupture of the aneurysm in this instance. The patient, a 35 year old white female, was notified of her father's death. Ten minutes later she was found dead in the bathroom.

Pathological Features: Type of aneurysm. In six of the cases, two aneurysms were found yielding a total of 42 aneurysms in the 36 cases of the series. Twenty-two were found at the bifurcation of the vessels of the base and conform to the description of the typical "berry" aneurysm. Mycotic aneurysms were seen in 11 cases. Of the remaining nine cases, six were arteriosclerotic, two syphilitic and one traumatic. The mycotic aneurysms may be divided into two groups. *Streptococcus viridans* subacute bacterial endocarditis provided the septic focus for seven aneurysms. *Staphylococ-*

cus aureus hemolyticus sepsis accounted for three others, and the fourth was seen in a case of influenzal meningitis.

CHART III

Sites of Aneurysm

Middle cerebral artery	10
Anterior communicating artery	8
Anterior cerebral	6
Internal carotid	5
Convexity	5
Basilar	3
Vertebral	2
Posterior communicating	1
Posterior cerebral	1
Anterior inferior cerebellar	1
Total	42

Site of aneurysm. In chart 3 is listed the incidence of the aneurysms on the various branches of the Circle of Willis. Those occurring on the convexity of the brain were invariably of the mycotic type, and were found in each instance incidentally either grossly or on section through a focal area of subarachnoid hemorrhage. It should be stressed that whenever a zone of subarachnoid hemorrhage was seen in a case of meningitis or sepsis, section was taken for microscopic study, thus accounting for a high incidence of mycotic aneurysms.

A method employed by the authors in identifying the site of rupture in those cases where no definite aneurysmal sac was seen in the basilar vessels was suggested by Dr. Richard Grimes, Assistant Medical Examiner, and seems worthy of comment. At times, after careful dissection of the vessels and removal of the entire blood clot cast from the subarachnoid space, a ragged zone was seen in a portion of a vessel with adherent blood clot. If a closed circuit is made by means of clamps, and water is injected under moderate pressure, the site of rupture is then indicated by escape of a thin stream of water. Two instances of rupture of the vertebral artery were demonstrated by this method.

Size. The smallest aneurysm in the series was 2 mm. in diameter, whereas the largest measured 4 by 4 cm. The majority varied from 3 to 10 mm. in size.

Sites of hemorrhage. In each case of ruptured aneurysm recorded, there was seen subarachnoid hemorrhage which varied in amount. In some of the small mycotic aneurysms, hemorrhage of a focal nature was seen usually over the convexity of the cerebrum. In the cases of rupture of the vessels comprising the Circle of Willis, blood clot casts of the subarachnoid space and the cisternae at the base of the brain were seen. In 10 cases *intracerebral hemorrhage* of varying degree was noted. This form of hemorrhage likewise varied from small zones to extensive areas, the largest measuring 8 by 6 by 4 cm. The location of the zones of intracerebral hemorrhage were as

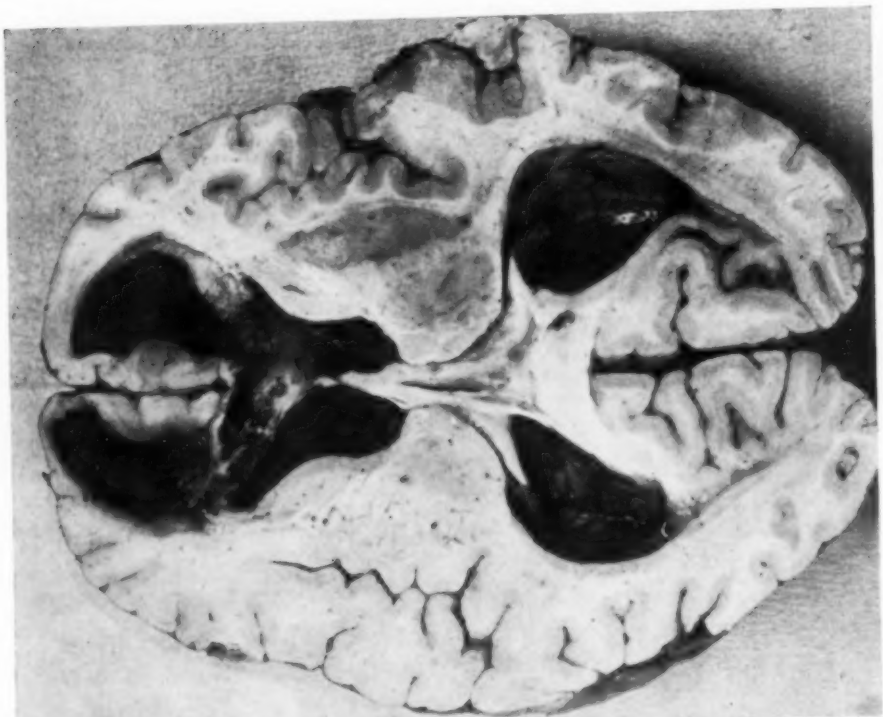

FIG. 2. *Case 1.* Symmetrical bilateral hemorrhage into frontal lobes suggesting slow ooze from ruptured symmetrically placed aneurysms (see figure 1). Note terminal ventricular extension.

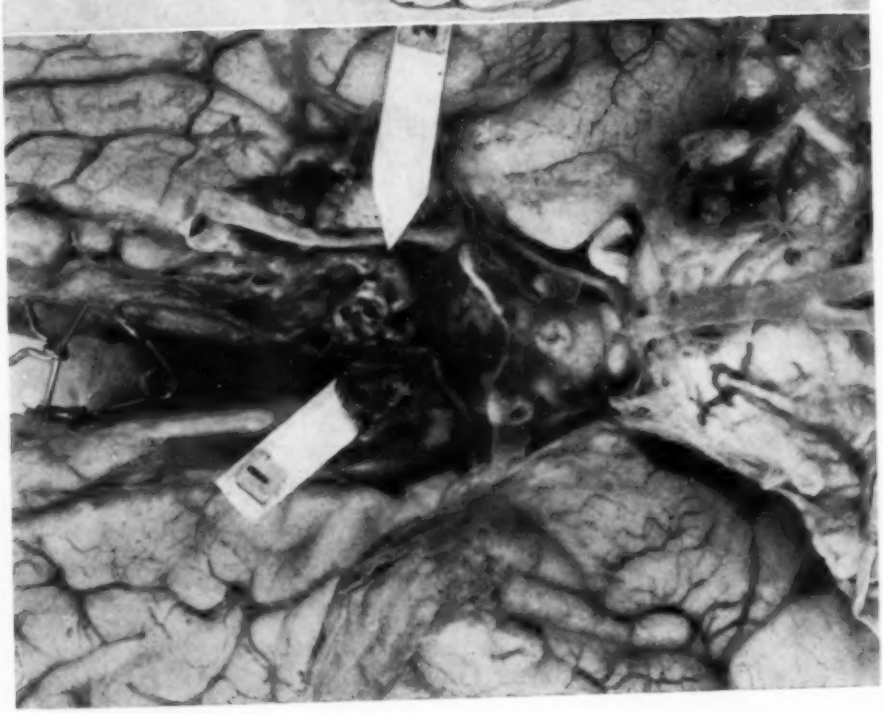

FIG. 1. *Case 1.* View of base of brain. Arrow 1 below ruptured "berry" aneurysm of right anterior cerebral artery. Arrow 2 points to symmetrically placed ruptured aneurysm of left anterior cerebral artery. Note limited regional subarachnoid hemorrhage.

follows: frontal lobe (4), temporal lobe (2), basal ganglia (3), and corpus callosum (1). All of the frontal lobe hemorrhages were associated with aneurysms of the anterior cerebral arteries, case 1 (figures 1 and 2), case 2 (figures 3 and 4). The temporal lobe hemorrhages followed a rupture of aneurysms in the middle cerebral arteries, case 5 (figure 8). Intraventricular extension of the hemorrhage was found in 11 cases. One of the 11 cases presented only intracerebral hemorrhage associated with bleeding extending to the ventricles. Five were associated with subarachnoid hemorrhage only, and the remaining five were found in cases showing both intracerebral and subarachnoid hemorrhage.

Associated pathological findings. Hypertrophy of the heart was found in the nine cases which showed evidence of hypertension clinically, or with a history of hypertension. Case 3 presented other congenital anomalies associated with the berry aneurysm. Large polycystic kidneys and multiple cysts of the liver were noted in this instance. O'Crowley and Martland [6] have noted this association of polycystic kidneys with the so-called congenital aneurysms of the cerebral vessels. For the congenital feature to be significant, hypertension should be ruled out. He also stressed the occasional occurrence of status thymolymphaticus. In two of our cases, cases 30 and 33, variable amounts of thymic tissue were found. In case 30, a hypoplastic aorta and adrenal cortex were seen. In case 33 the alleged typical appearance of status was present. The patient was a red-headed, fair-skinned individual with a large thymus and hypoplastic aorta and cerebral vessels. In case 35 the patient had extensive Paget's disease of the skull. The history in this case was of interest for its medico-legal implications. The patient, a 52 year old female, was found dead at the foot of a flight of stairs. A large laceration of the scalp was seen. Upon reflecting the scalp a large linear fracture of the skull was noted. Careful dissection of the brain, however, revealed extensive subarachnoid hemorrhage from a ruptured arteriosclerotic aneurysm of the basilar artery. The two cases of ruptured syphilitic aneurysm of the cerebral vessels were accompanied by evidence of active syphilis of the meninges, cerebral vessels, and brain. In case 7 multiple miliary gummata of the kidney were found in addition to active syphilitic hepatitis with cirrhosis. In case 23 a gross diagnosis of berry aneurysm was made, but microscopy revealed active cerebral meningovascular syphilis and gummatous necrosis of the wall of the aneurysm.

It is noteworthy that of the 11 mycotic aneurysms only three organisms were found on culture in various sites. The *Streptococcus viridans* was found in seven instances, all these cases presenting a classical picture of subacute bacterial endocarditis. The other organisms implicated were the *Staphylococcus aureus hemolyticus* and *Hemophilus influenzae.* In two of the cases the immediate seeding focus for the sepsis was the presence of multiple kidney abscesses. The third case was one of cavernous sinus thrombosis.

extension.
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left anterior cerebral artery. Note limited regional subarach-

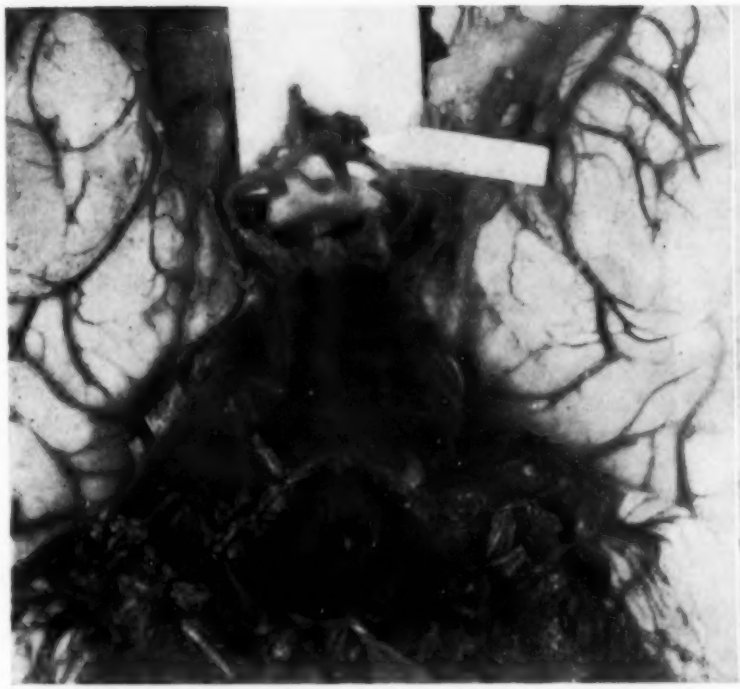

FIG. 3. *Case 2.* Base of brain showing massive subarachnoid hemorrhage in inter-peduncular space and about pons with limited extension to cerebellum. Arrow points to site of rupture of "berry" aneurysm of anterior communicating artery.

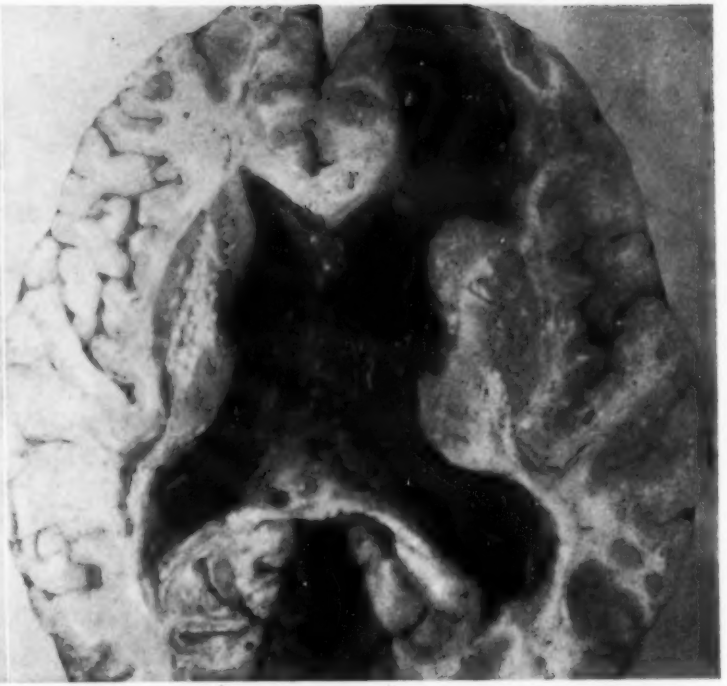

FIG. 4. *Case 2.* Unilateral frontal lobe hemorrhage suggesting slow ooze from aneurysm (see figure 3), with terminal massive ventricular extension.

Cerebral arteriosclerosis of all of the basilar vessels was described as marked in four of the cases and moderate in three. Of these seven cases, it should be noted that only three were instances of arteriosclerotic aneurysms whereas the remaining four showed the classical picture of "berry" aneurysm.

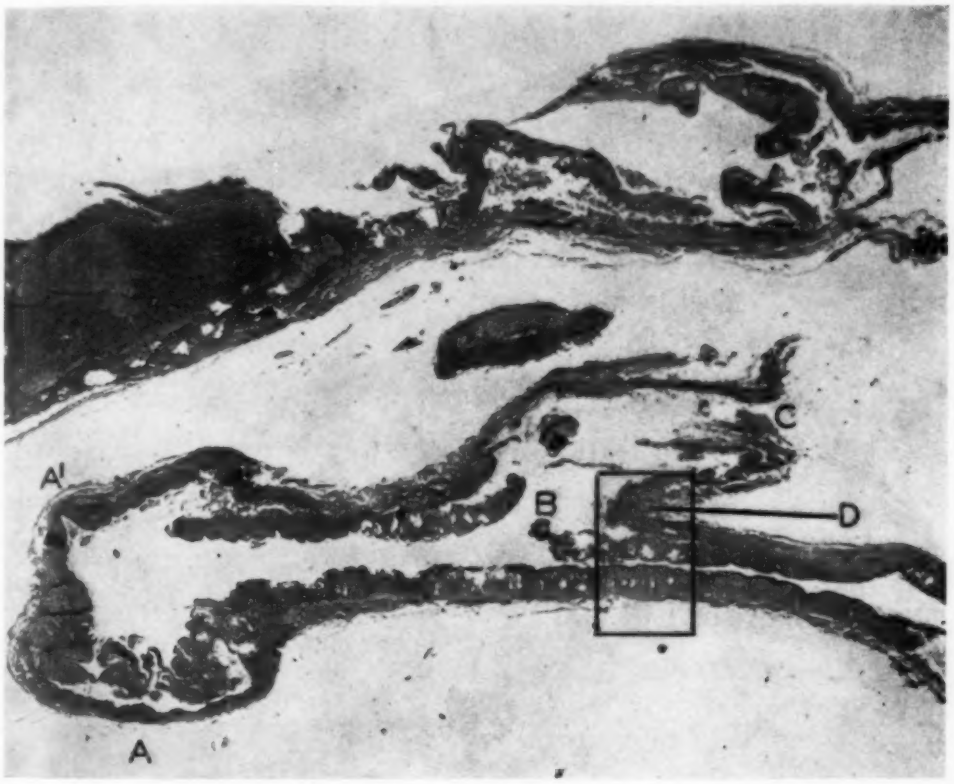

FIG. 5. *Case 3.* Longitudinal section of vertebral artery with multiple "berry" aneurysms, one showing site of rupture. A and A^1—unruptured aneurysms. B—neck of ruptured aneurysm. C—site of rupture. D—necrosis of arterial wall, enlarged in figure 6. Remnant of pia-arachnoid with subarachnoid hemorrhage at upper left margin. L. P. 48 mm.

Microscopic observations and discussion. Histological preparations of aneurysms were available in 25 of the 36 cases included in the series. All of the mycotic aneurysms were confirmed by section. The diagnosis of syphilitic aneurysm was established by the microscopic study, though the gross opinion was congenital aneurysm. It is our opinion that all aneurysms must be studied histologically to confirm the gross diagnosis in order to rule out complicating associated pathology of this type. Seven of the 12 ruptured "berry" aneurysms were studied in microscopic section. Hematoxylin and eosin stains were used routinely, with only an occasional elastic tissue stain. Defect of the media with loss of the muscle coat was commonly present in the "berry" group.

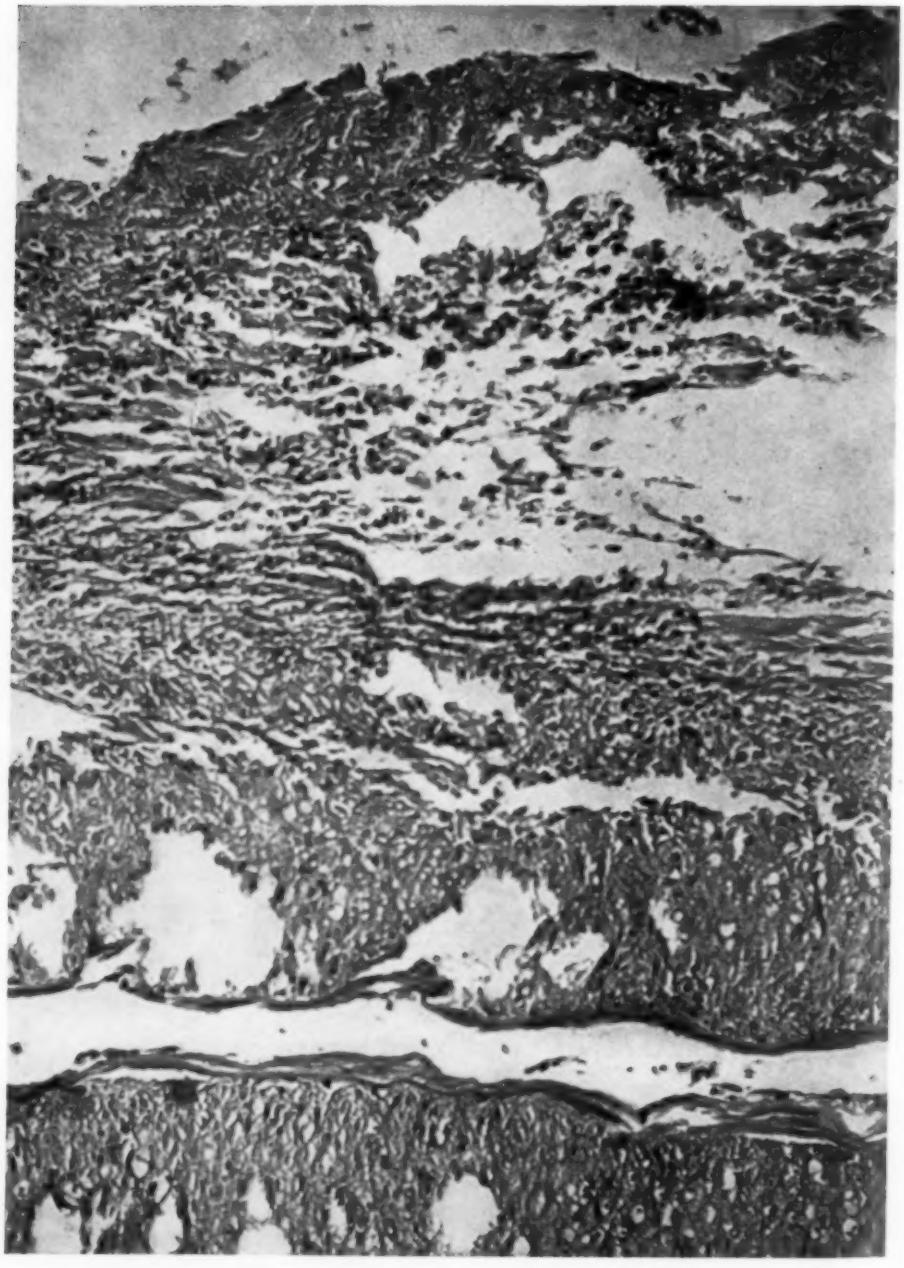

FIG. 6. *Case 3.* Higher magnification of insert in figure 5 through neck and wall of aneurysm showing necrosis and extensive acute inflammatory reaction at D (H. P. 8 mm.).

Certain facts stand out in this microscopic survey. Contrary to the original impression before initiating this study, there was found an unexpected degree of arteriosclerosis in the wall of the "berry" aneurysms. In the seven cases of this group in which sections were studied, five were under the age of 50. Case 2 was 12 years old and showed swelling and thickening of the elastic membrane. No other evidence of arteriosclerosis was present. Case 34, a 35 year old white woman, showed an inordinate degree of atheroma, thickening and hyalinosis of all coats and distortion of the vessel by eccentric thickening and thinning of the wall. It is significant that the remainder of the basilar vessels in this case were unusually free of atherosclerotic change. Cases 12 and 28 showed marked atherosclerosis and hyaline fibrosis of the wall, limited to the aneurysmal wall. The presence of such advanced local changes in the aneurysms precludes any definite statement as to the existence or absence of elastica within the aneurysmal sac. The absence of sclerotic changes in the basilar vessels outside of the aneurysm in the younger age group is of importance. Glynn demonstrated that weakening or rupture of the cerebral vessels failed to occur as long as the elastica remained intact. The disruption of the elastica in arteriosclerosis may offer one additional factor for explanation of rupture of the "berry" aneurysms. Schmidt [7] emphasized this point in the following statement: "In others of my cases, the wall of the aneurysm has shown obviously arteriosclerotic changes, while the rest of the cerebral vessels did not reveal any sign of arteriosclerosis on microscopic examination." Strauss et al.[8] also stressed the finding of focal arteriosclerotic changes in the "region of the aneurysms."

Case 3 is of particular interest. The finding of an extensive zone of necrosis within the wall of the vessel at the neck of the aneurysm with an acute inflammatory reaction (figures 5 and 6) suggests the mechanism of rupture. The reaction seems out of proportion to the degree of vital reaction which might be expected to follow upon spontaneous mechanical rupture of the vessel wall. This finding intimates some other unknown etiological factor in the production of the necrosis in the vessel wall with subsequent rupture. Although the finding of the non-specific necrosis in this case is an isolated one in the series, it presents a morphological demonstration of that additional mechanism thought necessary for rupture suggested by Richardson and Hyland.

In the two syphilitic cases, gummatous necrotic destruction of the wall accounted for the rupture in a similar fashion. A similar zone of necrosis was found in the wall of the internal carotid artery at the site of a traumatic arteriovenous aneurysm (case 10). In the mycotic group, necrosis of the vessel wall including the elastica, was verified in all cases as the cause of the aneurysm and the rupture (figure 9).

It is possible that some of the arteriosclerotic aneurysms found in the older age groups might represent sclerotic changes in preëxisting "berry"

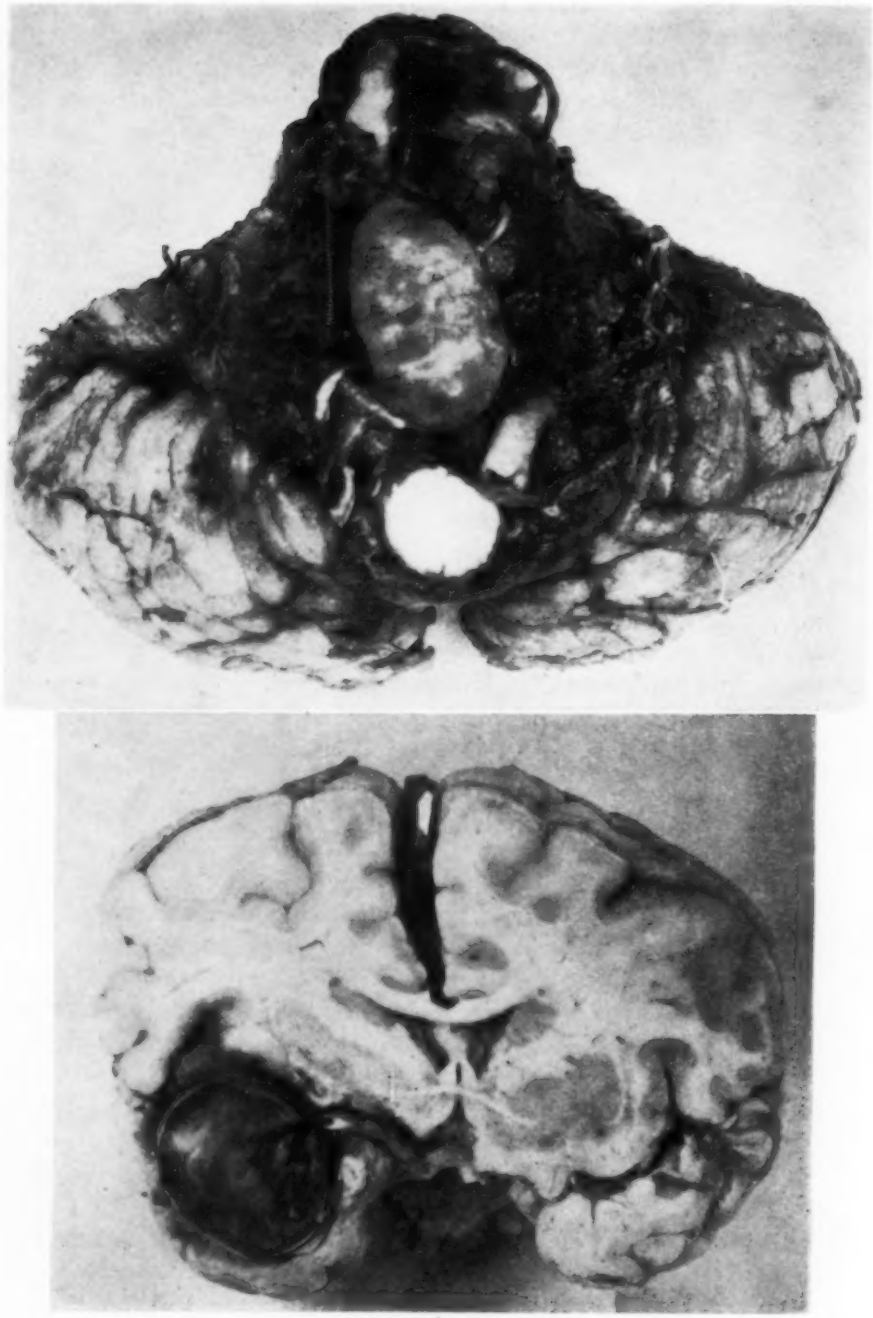

FIG. 7. (*Above*) *Case 4.* Base of brain stem and cerebellum showing fusiform arteriosclerotic aneurysm of basilar artery and extensive subarachnoid hemorrhage.

FIG. 8. (*Below*) *Case 5.* Coronal section of cerebrum showing large saccular arteriosclerotic aneurysm of right middle cerebral artery deeply embedded in temporal lobe.

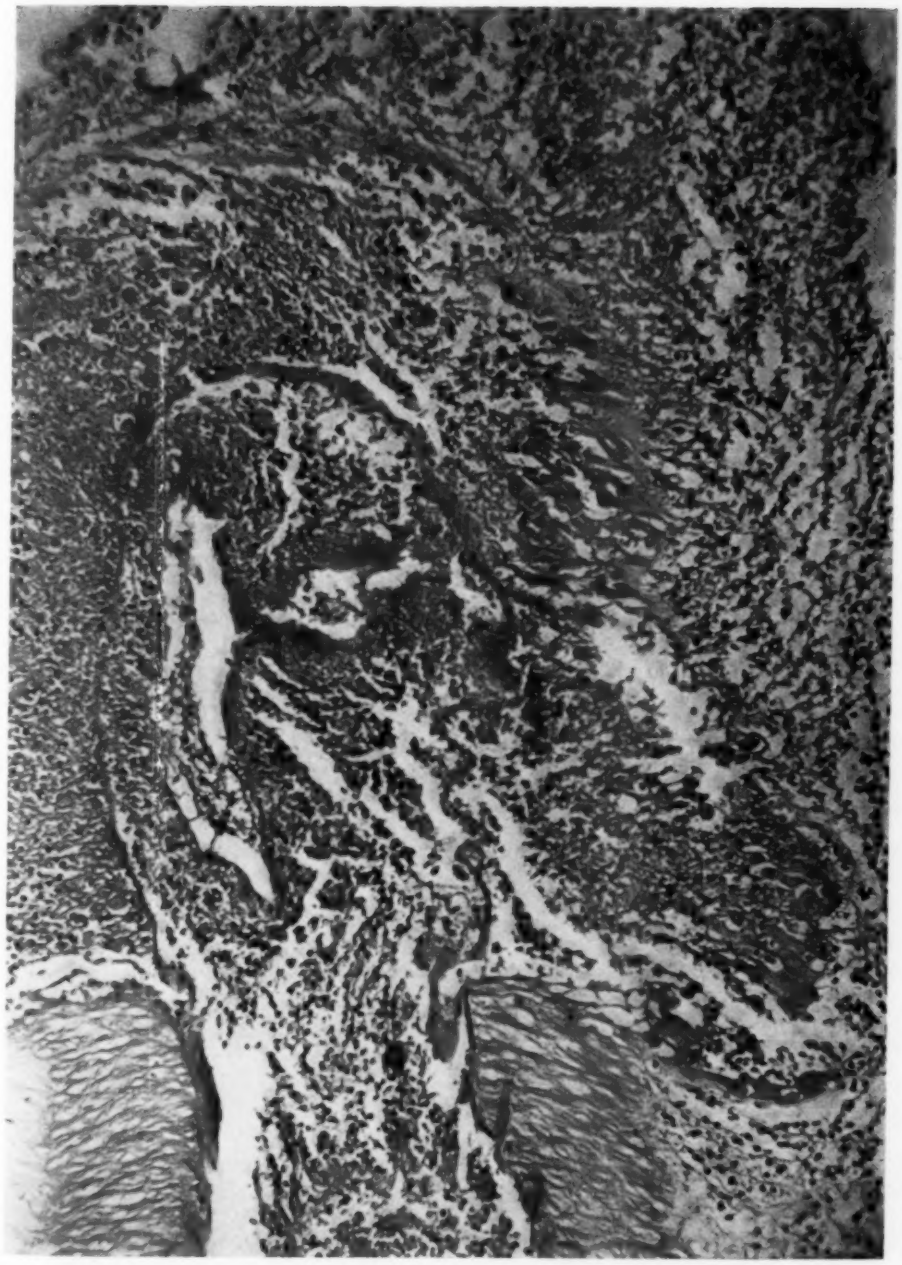

FIG. 9. *Case 6.* Mycotic aneurysm of small leptomeningeal vessel in a case of cavernous sinus thrombosis showing intact vessel wall below, and necrosis and marked acute inflammation above (H. P. 8 mm.).

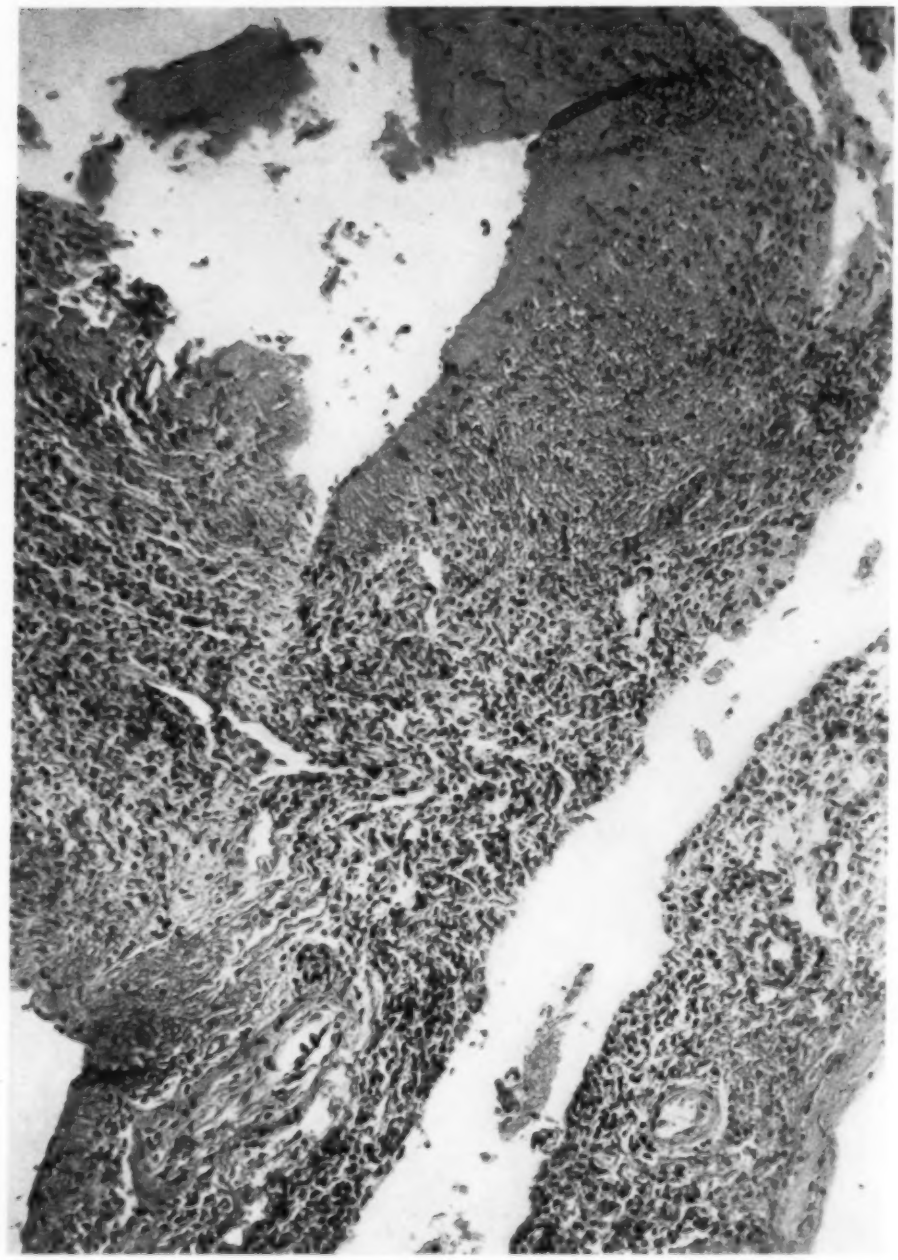

FIG. 10. *Case 7.* Gummatous lesion of wall of ruptured aneurysm of left internal carotid artery and adjacent pia-arachnoid in a case of active meningo-vascular syphilis (L. P. 16 mm.).

aneurysms. In this paper, such instances are listed as arteriosclerotic if marked arteriosclerosis of the cerebral vessels was present. The saccular aneurysm seen in case 5 (figure 8) and the fusiform sac seen in case 4 (figure 7) probably do represent true arteriosclerotic aneurysms because of their location and size.

It is of interest and worthy of reiteration that once the aneurysmal pouch is formed, local vascular disease in the form of atheroma, sclerosis or actual necrosis seems to predominate in the defective part of the vessel.

Summary and Conclusions

1. Thirty-six cases of intracranial aneurysms of the cerebral arteries are presented.

2. Forty-two aneurysms are included, subdivided as follows: "berry" 22, mycotic 11, arteriosclerotic 6, syphilitic 2, traumatic (arterio-venous) 1.

3. The presence of arteriosclerosis and of necrosis in the wall of the aneurysm is stressed in the mechanism of rupture.

4. On the basis of the recorded observations, careful histological study of all ruptured and unruptured aneurysms for evidence of atherosclerosis, for active degeneration and necrosis, and for evidence of specific and non-specific inflammation, is indicated for the further elucidation of this problem.

The authors wish to thank Dr. Richard Grimes, Assistant Medical Examiner, for the opportunity of studying much of the material contained in this paper.

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THE DIAGNOSTIC QRS PATTERNS IN MYOCARDIAL INFARCTION *

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In the electrocardiographic diagnosis of recent myocardial infarction, so much emphasis has been placed on the S–T–T configuration, because of the diagnostic value of its evolution, that the importance of the QRS pattern has been insufficiently stressed. Recent experience has shown that several conditions such as acute diffuse pericarditis,[1] acute cor pulmonale,[2] acute nephritis,[3] toxemias of pregnancy,[4] hyperthyroid state in flux,[5] etc., may sometimes closely imitate the S–T–T pattern of myocardial infarction and less closely its evolution, without showing the specific QRS patterns expected in myocardial infarction. It therefore seemed desirable to investigate the QRS patterns encountered in recent myocardial infarction in greater detail, with the thought in mind that such knowledge would increase the ability to use the electrocardiogram in differential diagnosis. Although some studies on QRS patterns in myocardial infarction have appeared in the past,[6] they have been incomplete for the most part.

The present study is based on an analysis of serial records in 369 cases selected from the files of the Heart Station covering the past six years. In obtaining these data some 800 series of records classed in the files as indicative of myocardial infarction were examined. All cases in which there was the slightest doubt as to the electrocardiographic diagnosis were discarded, even when, as was true in many instances, the clinical picture was unequivocal. We doubtless discarded many cases of recent myocardial infarction in this way. However, since we were interested in establishing the electrocardiographic patterns characteristic of myocardial infarction, the non-characteristic changes in cases known to have recent myocardial infarction clinically would not be of value in utilizing the electrocardiogram as an independent objective diagnostic procedure. It is noteworthy that of the 369 cases of this series in 36 in which necropsies were available the diagnosis of the presence and location of the infarct was confirmed. All 369 cases in this study had chest leads; approximately 75 per cent had both chest leads CF_2 and CF_4, the remaining 25 per cent having only chest lead CF_2. Most of the cases had long series of records, some with controls before, and more with records after stabilization had been completed. In a few instances, cases with single records were included, but only when they were absolutely typical. The use of serial records and chest leads, as emphasized before, is of considerable

* Received for publication September 4, 1942.
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Aided by the Emil and Fanny Wedeles and the A. D. Nast Funds for Cardiovascular Research.

aid in diagnosing recent myocardial infarction, and reliance on single limb lead records, except in unusual circumstances, may be misleading.

The distribution of the cases into types based on both the S–T–T and QRS patterns is shown in table 1. The most significant analysis revealed in this study was the limb lead QRS patterns in anterior wall infarction; but, before presenting this, our findings in the other patterns merit brief comment.

TABLE I

Distribution of the 369 Cases of the Series into Types Based on the S-T-T and QRS Configuration

Pattern	No. of Cases	% of Cases
Anterior wall	190	51
Posterior wall	141	38
Combined anterior and posterior wall	20	6
Atypical	18	5
Totals	369 cases	100%

It was noted, incidentally, that T-wave inversions occurring at some time during the evolution in all three limb leads (T_N type) [7] were found in 41 of the 369 cases (11 per cent). This was more frequent in the combined and atypical infarct pattern groups (45 per cent and 28 per cent respectively) than in the anterior or posterior wall patterns (7 per cent and 9 per cent respectively). This compares reasonably with a previous report,[7a] and the greater frequency of the T_N type in combined anterior and posterior wall patterns substantiates the concept that the T_N is evidence of a more widely distributed area of infarction.

Evidence of acute diffuse pericarditis complicating recent infarction [8] was diagnosed in the electrocardiogram in 13 cases, nine with anterior (5 per cent) and four with the posterior wall patterns (3 per cent). The diagnosis was made only in cases of these two infarct patterns when S–T was elevated in all three limb leads for a time, or when marked S–T elevation occurred in two limb leads and the S–T segment was not depressed in the third limb lead. Obviously, this diagnosis was not attempted in instances of atypical or combined infarct patterns.

The 18 cases classed as atypical infarct patterns (table 1) did not fall into the patterns of anterior, posterior, or combined infarcts, but represent true instances of myocardial infarction, as their S–T–T evolution was characteristic in showing waxing and waning of the T waves and restoration of the deviated S–T segments toward normal. They may represent examples of small atypically located infarcts, but no autopsy findings were available. Obviously an analysis of their QRS patterns in our present state of knowledge would not be of much value and was therefore not attempted.

In 20 cases patterns were encountered having some characteristics of anterior and others of posterior wall infarction. In two of these postmortem findings revealed the presence of infarction in both localities; in one

both were recent, in the second the two were of different ages. It is probable that some of these 20 cases represent recent infarction in one locality superimposed on an old infarct in the other, whereas others represent simultaneously occurring infarcts in both areas. It is also possible that large lateral wall infarcts extending to both regions may account for some of these cases. The diagnosis was made in this group on the configuration of the QRS as well as that of the S–T–T in both the limb and chest leads. When the dominant pattern in the limb and the dominant one in the chest leads were analyzed, it was found that in 15 of the cases (75 per cent) the limb leads had a predominantly posterior wall pattern while the chest leads had a predominantly anterior wall pattern. In only one case was the reverse true. In the remaining four it was not possible to speak of a dominant pattern in either the chest or limb leads, the admixture being equally distributed between anterior and posterior wall characteristics. Knowledge of the QRS patterns encountered in anterior and posterior wall infarction was useful in this classification, and their evaluation is therefore valuable in recognizing atypical and combined types of infarction contours.

Posterior Wall Patterns

There were 141 cases showing patterns indicative of posterior wall infarction. In four of these, two types of limb lead QRS patterns were found in the serial records of the cases, making a total of 145 limb lead QRS patterns for analysis. The distribution of these limb lead QRS patterns is

Table II

Frequency of Various Types of QRS Patterns in the Limb Leads Encountered in Posterior Wall Infarction

Pattern	No. of Cases	% of Cases
Diphasic QRS with deep Q waves in Leads II and III	61	42
Triphasic QRS with deep Q waves in Leads II and III	3	2
Triphasic QRS_2 and diphasic QRS_3 with deep Q waves	2	1
Diphasic QRS_2 with deep Q and QRS_3 entirely inverted	13	9
Triphasic QRS_2 with deep Q and QRS_3 entirely inverted	17	12
Triphasic QRS_2 with deep Q and M-shaped QRS_3	1	½
QRS entirely inverted in Leads II and III	7	5
Diphasic QRS_3 with deep Q and QRS_2 normal	26	18
Triphasic QRS_3 with deep Q and QRS_2 normal	1	½
All other cases not falling into any of above categories	14	10
Totals	145	100
Low "voltage"	20 cases	14%
Intraventricular block	12 cases	9%

shown in table 2. It will be seen that in 89 of the 145 instances (61 per cent) a diphasic QRS_3 with a Q wave 25 per cent or more of the upright phase (the so-called diphasic Q_3 pattern) was present (figure 1); in 61 of these a similar diphasic Q pattern occurred in Lead II. Further examination revealed that in all except 14 of the 145 cases equivalents of the diphasic Q

pattern were present in Lead II, Lead III, or both (table 2). These equivalents consisted of (a) a triphasic W-shaped QRS with a first inverted phase 25 per cent or more of the upright phase, the so-called triphasic Q_2 and Q_3 patterns (figure 1), and (b) entirely inverted QRS_3 with diphasic or tri-

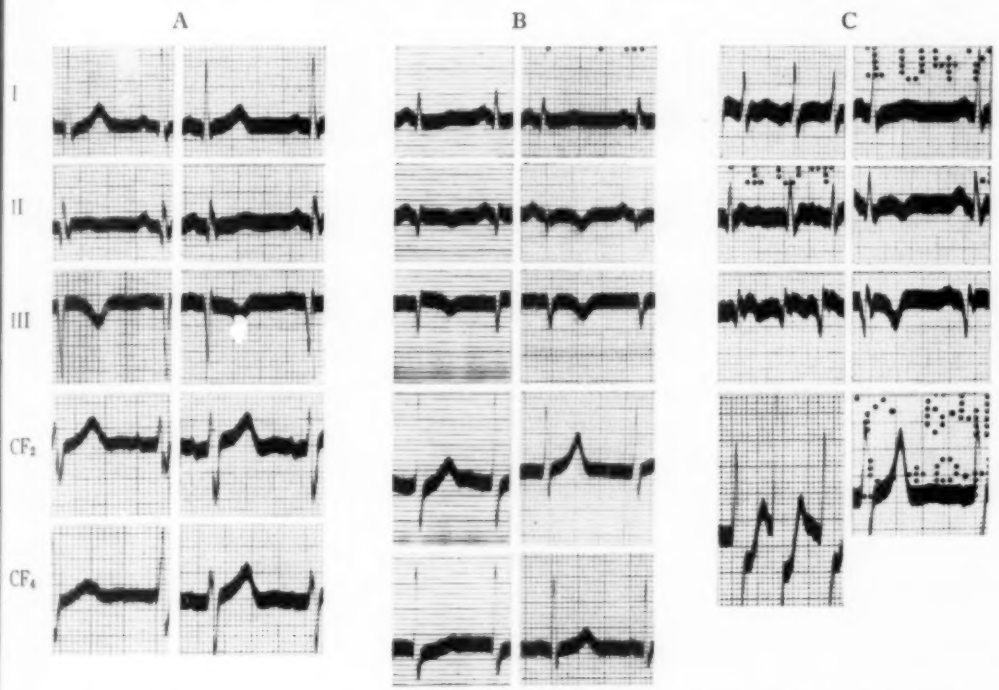

FIG. 1. Three cases of posterior wall infarction to illustrate the diphasic Q type of QRS in Leads II and III and its variants, the triphasic W-shaped QRS and the entirely inverted QRS. The latter in Lead III has the same significance as a Q type only when QRS_2 is of the diphasic or triphasic Q type. Discussed in text.

A. An example of a triphasic QRS_2 of the Q type and QRS_3 entirely inverted (in the first record), the latter subsequently changing to a diphasic Q type (in the second record). The two records were taken a year apart in a case with a recent myocardial infarction developing five days before the first record.

B. An example of a diphasic Q type of QRS_2 (in the first record), becoming a triphasic W-shaped QRS (in the second record) and a diphasic Q type of QRS_3 becoming an entirely inverted complex. The two records were taken 15 days apart in a case with a recent myocardial infarction developing one day before the first record.

C. An example of a diphasic Q type of QRS_3 (in the first record) becoming a triphasic Q type (in the second record). Note the auricular fibrillation present in the first record. The two records were taken five weeks apart in a case with a recent myocardial infarction developing six days before the first record.

phasic Q patterns in Lead II or QRS_2 inversion. The correctness of the interpretation that these are diphasic Q equivalents was shown by their serial evolution from or into the more typical patterns (figure 1). Although the diagnosis could almost always be made from the S–T–T pattern and its evolution, the fact that the Q pattern may remain when the S–T–T has lost its characteristics makes the diphasic Q pattern or its equivalent significant

not only in the diagnosis of recent infarction but also in indicating the presence of an old infarct, particularly when QRS_2 as well as QRS_3 shows the Q pattern or its equivalent (figure 1 A). It has been our custom in these cases, therefore, not to consider inverted QRS_3, or QRS_2 and QRS_3, as being indicative of left ventricular preponderance in the absence of deep S waves, the QRS inversion being ascribed to the recent or old infarct per se. Conditions other than infarction, notably obesity and right ventricular hypertrophy, may show a Q_3 pattern, but in such cases no Q_2 pattern is found.

The chest lead changes were not as significant in the diagnosis of posterior wall infarction as in the anterior wall type, but often aided considerably in showing depressed S–T segments in the acute stage and waxing T waves in the healing stage of infarction (figure 1 C). In only two instances were the chest leads characteristic of infarction in the presence of noncharacteristic limb lead changes, this being in sharp contrast to the anterior wall type in which 9 per cent of our cases showed pathognomonic chest lead changes in association with non-specific limb lead abnormalities. In most cases, however, the chest lead QRS was of normal configuration (being, of course, prolonged in the 12 cases with intraventricular block, and occasionally showing low "voltage" when the limb leads did also). In only 13 cases was QRS in CF_2 mainly upright with a small final phase (less than five mm.) which is abnormal [9] (figure 1 B).

In 10 cases autopsy studies were available and the expected infarction was found in all.

The appearance of a deep S wave in Lead I as a concomitant finding with a Q_3 pattern (figure 1 C) was found in only 17 cases and is, therefore, statistically not of great significance. Nevertheless, its occasional occurrence in posterior wall infarction is of moment since failure to appreciate this may lead to attributing it to some other cause. The S_1 and Q_3 combination is much more significant in the diagnosis of pulmonary embolism and is almost pathognomonic when associated with the characteristic S–T–T changes of this state.

Anterior Wall Patterns

Unlike posterior wall infarction, the presence of a Q pattern is not so common in anterior wall infarction. In this series, a QRS_1 with a deep Q wave was encountered in only 54 of the 190 cases (28 per cent), in 37 instances the QRS_1 being diphasic and in 17 the triphasic W-shaped equivalent (figure 7 B). Just as in the posterior wall infarction pattern, so also in the anterior, the entirely inverted QRS_1 with (figure 7 B) or without (figure 7 D) notching on its downstroke was found, but here in only eight instances. In nine cases a Q_2 pattern or its equivalent as well as a Q_1 pattern was found.

It is obvious that reliance only on the presence of the pathognomonic Q_1, or Q_1 and Q_2 patterns, was helpful in only a little over 25 per cent of the cases. Reliance must therefore be placed on other characteristics of the QRS if its contour in the limb leads is to be of value. The series of 190

cases of anterior wall infarction was, therefore, reëxamined for other patterns which might be of diagnostic significance. In this analysis the cases with Q_1, or Q_1 and Q_2 patterns, were lumped together with those not showing them; cases with low "voltage" and intraventricular block (QRS duration 0.12 second or more) were not excluded.

This breakdown showed five distinct limb lead QRS patterns besides a miscellaneous group. In table 3 are shown the characteristics and frequency

TABLE III

Description and Frequency of the Various Types of QRS Patterns in the Limb Leads Encountered in 194 Combinations in 190 Cases of Anterior Wall Infarction Patterns

Type	Description	No. of Cases	% of Series	No. Cases with Low "Voltage"	No. Cases with Q_1 Pattern*	No. Cases with Intraventricular Block†
I	QRS_1 relatively small and upright, QRS_2 and QRS_3 diphasic and mainly or almost entirely inverted with deep S waves which are larger than QRS_1	35	18	2	19	13
II	QRS_2 and QRS_3 similar to type I, but QRS_1 upright and relatively normal in size	28	14	4	5	4
III	QRS_1 relatively small and upright, QRS_2 and QRS_3 entirely or mainly upright	15	8	2	7	0
IV	QRS_1 small and equiphasic, or mainly or entirely inverted; QRS_2 mainly or entirely upright; QRS_3 upright, equiphasic, or inverted	14	7	3	7	0
V	QRS mainly or entirely inverted in all three limb leads	4	2	3	1	1
All other cases not falling into any of the above groups		98	51	17	15	13
Totals: No. of cases % of entire series		194	100%	31 16%	54 27%	31 16%

* Described in text.
† QRS in limb leads 0.12 sec. or more.

of each, as well as the number of instances with Q_1 patterns, with low "voltage," and with intraventricular block. In 186 of the cases only one QRS type was found in the serial curves, but in four, two patterns were revealed, making a total of 194 patterns in the 190 cases.

As table 3 will show, the relatively small QRS_1 is the common attribute in types I and III and constitutes the abnormality in 50 cases. When to these are added the instances of small equiphasic or inverted QRS_1 common to types IV and V, which are the other varieties of abnormal QRS_1 en-

not only in the diagnosis of recent infarction but also in indicating the presence of an old infarct, particularly when QRS_2 as well as QRS_3 shows the Q pattern or its equivalent (figure 1 A). It has been our custom in these cases, therefore, not to consider inverted QRS_3, or QRS_2 and QRS_3, as being indicative of left ventricular preponderance in the absence of deep S waves, the QRS inversion being ascribed to the recent or old infarct per se. Conditions other than infarction, notably obesity and right ventricular hypertrophy, may show a Q_3 pattern, but in such cases no Q_2 pattern is found.

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Anterior Wall Patterns

Unlike posterior wall infarction, the presence of a Q pattern is not so common in anterior wall infarction. In this series, a QRS_1 with a deep Q wave was encountered in only 54 of the 190 cases (28 per cent), in 37 instances the QRS_1 being diphasic and in 17 the triphasic W-shaped equivalent (figure 7 B). Just as in the posterior wall infarction pattern, so also in the anterior, the entirely inverted QRS_1 with (figure 7 B) or without (figure 7 D) notching on its downstroke was found, but here in only eight instances. In nine cases a Q_2 pattern or its equivalent as well as a Q_1 pattern was found.

It is obvious that reliance only on the presence of the pathognomonic Q_1, or Q_1 and Q_2 patterns, was helpful in only a little over 25 per cent of the cases. Reliance must therefore be placed on other characteristics of the QRS if its contour in the limb leads is to be of value. The series of 190

cases of anterior wall infarction was, therefore, reëxamined for other patterns which might be of diagnostic significance. In this analysis the cases with Q_1, or Q_1 and Q_2 patterns, were lumped together with those not showing them; cases with low "voltage" and intraventricular block (QRS duration 0.12 second or more) were not excluded.

This breakdown showed five distinct limb lead QRS patterns besides a miscellaneous group. In table 3 are shown the characteristics and frequency

TABLE III

Description and Frequency of the Various Types of QRS Patterns in the Limb Leads Encountered in 194 Combinations in 190 Cases of Anterior Wall Infarction Patterns

Type	Description	No. of Cases	% of Series	No. Cases with Low "Voltage"	No. Cases with Q_1 Pattern*	No. Cases with Intraventricular Block†
I	QRS_1 relatively small and upright, QRS_2 and QRS_3 diphasic and mainly or almost entirely inverted with deep S waves which are larger than QRS_1	35	18	2	19	13
II	QRS_2 and QRS_3 similar to type I, but QRS_1 upright and relatively normal in size	28	14	4	5	4
III	QRS_1 relatively small and upright, QRS_2 and QRS_3 entirely or mainly upright	15	8	2	7	0
IV	QRS_1 small and equiphasic, or mainly or entirely inverted; QRS_3 mainly or entirely upright; QRS_2 upright, equiphasic, or inverted	14	7	3	7	0
V	QRS mainly or entirely inverted in all three limb leads	4	2	3	1	1
All other cases not falling into any of the above groups		98	51	17	15	13
Totals: No. of cases % of entire series		194	100%	31 16%	54 27%	31 16%

* Described in text.
† QRS in limb leads 0.12 sec. or more.

of each, as well as the number of instances with Q_1 patterns, with low "voltage," and with intraventricular block. In 186 of the cases only one QRS type was found in the serial curves, but in four, two patterns were revealed, making a total of 194 patterns in the 190 cases.

As table 3 will show, the relatively small QRS_1 is the common attribute in types I and III and constitutes the abnormality in 50 cases. When to these are added the instances of small equiphasic or inverted QRS_1 common to types IV and V, which are the other varieties of abnormal QRS_1 en-

countered in anterior wall infarction, 68 of the 194 patterns are accounted for, a larger group than showed the Q_1 types. Relatively small and upright, small and equiphasic, or inverted QRS_1 are, therefore, more common concomitants of anterior wall infarction than the Q_1 pattern.

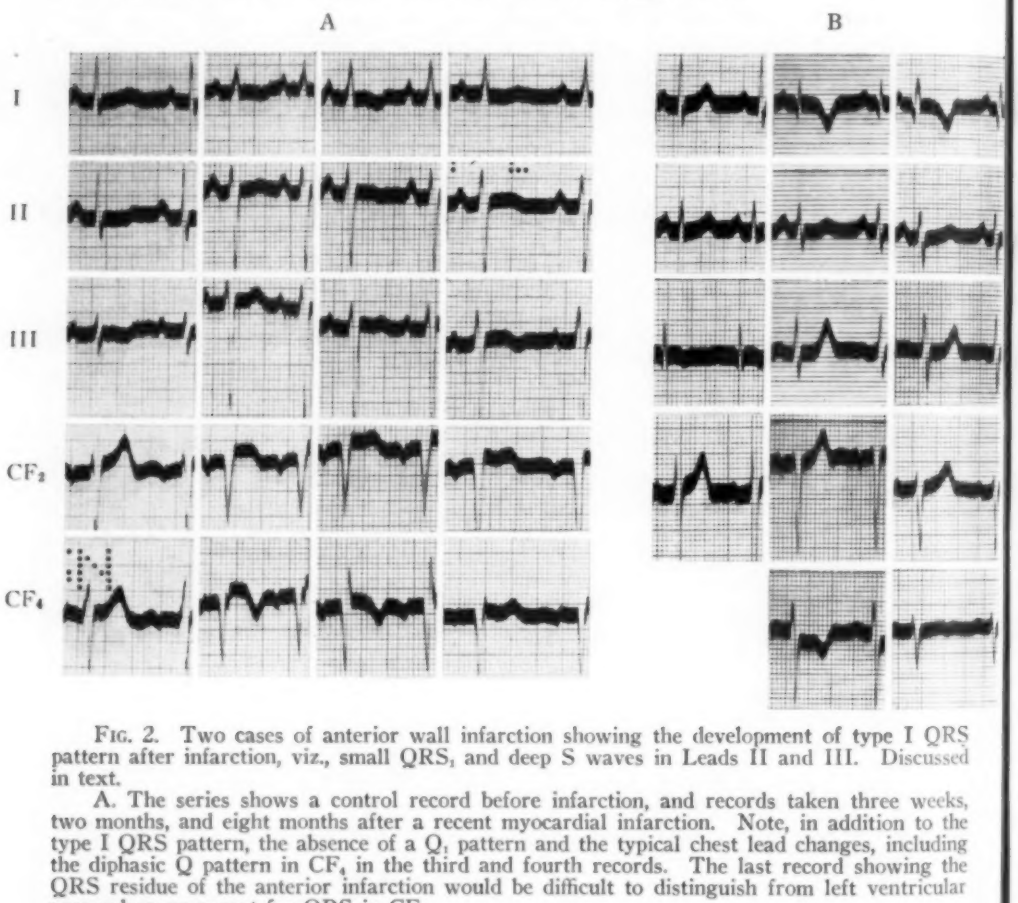

FIG. 2. Two cases of anterior wall infarction showing the development of type I QRS pattern after infarction, viz., small QRS_1 and deep S waves in Leads II and III. Discussed in text.

A. The series shows a control record before infarction, and records taken three weeks, two months, and eight months after a recent myocardial infarction. Note, in addition to the type I QRS pattern, the absence of a Q_1 pattern and the typical chest lead changes, including the diphasic Q pattern in CF_4 in the third and fourth records. The last record showing the QRS residue of the anterior infarction would be difficult to distinguish from left ventricular preponderance except for QRS in CF_4.

B. The series shows a control record before infarction and records taken the same day and three weeks after a recent myocardial infarction. Note, in addition to the type I QRS pattern, the Q_1 pattern and the non-characteristic QRS in the chest leads.

It is further significant that S_2 and S_3 occurred more frequently than the Q_1 type, viz., in 63 out of 194 patterns (types I and II of table 3). Furthermore, as table 3 shows, the S_2 and S_3 occur in the absence of the Q_1 types and, in type II, in the absence of small QRS_1. Thus it would appear that the S_2 and S_3 type is a more common concomitant of anterior wall infarction than the Q_1 type or the low and upright, low and equiphasic, or inverted QRS_1 contours; in fact, the number of cases showing S_2 and S_3 were equal to ¾ of the cases showing Q_1 types and/or low and upright, low and equiphasic, or inverted QRS_1, viz., 63 as against 88 cases respectively. In fact, in 21 cases

(in type II) the S_2 and S_3 were the only QRS pattern abnormalities, the QRS_1 being entirely normal.

A. Type I QRS of Anterior Wall Infarction. This type was first recognized as of diagnostic significance by Wilson et al.[6g] and by Winternitz [61] and has recently been stressed again.[10] Our study reveals it to be the most significant single variety since it combines the two common characteristics of anterior wall infarction, relatively small QRS_1 and deep S_2 and S_3 (figures 2, 3 and 5). Therefore, it merits consideration at some length.

The first question that arose was the extent to which this QRS pattern was attributable to the infarct. In six of the 35 cases in this group control records before the infarction occurred were available. In four of these the S-wave patterns were present in Leads II and III in the control records, being therefore attributable to preëxisting left ventricular preponderance. In these four cases, two showed deepening of the S waves after infarction (figure 2, A), and two did not, but in all four QRS_1, which was of normal size in the control records, decreased noticeably after the infarction. A like decrease in QRS_1 also occurred in the two other cases which had no S_2 and S_3 in the control records at the same time that the S_2 and S_3 appeared (figure 2, B). Thus it would seem that while preëxisting left ventricular preponderance may be responsible for the S_2 and S_3 in the type I QRS pattern after anterior wall infarction, this pattern can develop in some cases in the absence of left ventricular hypertrophy as a result of the infarct per se (figure 2, B). This latter view is supported by the fact that while 10 out of the 12 autopsied cases with this pattern showed left heart enlargement and hypertrophy as well as the anterior wall infarct, two others showed the infarct without any cardiac enlargement. It is, therefore, not justifiable to diagnose left ventricular hypertrophy when a type I QRS pattern is encountered in anterior wall infarction since the infarct itself may be the sole cause of the pattern.

This deduction is especially significant in the stage of stabilization of the record or later when the records have undergone restitution. At these times the S–T–T pattern may no longer be characteristic and the diagnosis of left ventricular preponderance alone might be entertained (figure 3). Six of the 35 cases fell into this category. In five of these cases the stabilized records resembled the mixed type of left ventricular preponderance [11] * in that with the deep S-waves in Leads II and III indicative of the first type, the S–T–T Lead I was indicative of the second type of left ventricular preponderance, viz., S–T was depressed and bowed upward and T was inverted and asymmetrical. While in all five QRS_1 had increased somewhat in size, in three it was sufficiently small still to fit the description of type I QRS of anterior wall infarction (figure 2, A). In the other two it was suf-

* In type I of left ventricular preponderance deep S-waves are present in Leads II and III. In type 2, a deep S_3 is present while $S\text{–}T_1$ is depressed, bowed upward, and T_1 is inverted or diphasic. In the mixed type, the characteristics of both the first and the second types are present. In all three types QRS_1 is tall.[9]

ficiently large to make the entire limb lead pattern indistinguishable from the classical mixed pattern of left ventricular preponderance (figure 3, B). The sixth case with complete restitution showed no abnormalities of the S–T–T at this time, and resembled the first type of left ventricular preponderance

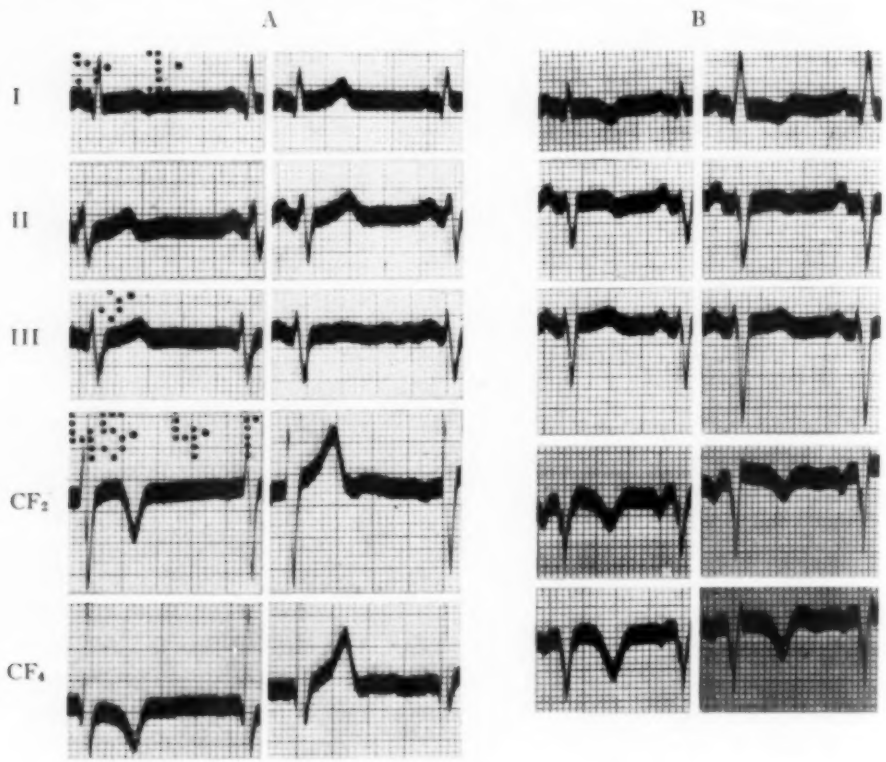

FIG. 3. Two cases of anterior wall infarction showing the type I QRS pattern, persisting in one (A) and changing to the type II in the other (B) after the record had stabilized. Discussed in text.

A. The two records were taken 14 months apart. The first was taken some time during the healing stage of the infarction. Note the atypical QRS patterns in the chest leads. In the second record only the type I QRS pattern (plus Q_1) remains as the residue of the infarction.

B. The two records were taken 11 months apart, the first being taken several weeks after the infarct developed. Note the persistence of the T-wave inversion in the chest leads and the persistence of the Q type QRS in these leads associated with the type II QRS pattern in the limb leads as the residue of the infarction. The S–T–T configuration in the limb leads suggests left ventricular preponderance.

except for the relatively small QRS_1 (figure 3, A). In five of these six cases the QRST pattern in the chest leads (CF_2 and CF_4) was of the type that we have come to recognize as characteristic of a recent or as the residue of an old anterior wall infarct [9] so that the true nature of the limb lead QRS changes was indicated (figures 2, A and 3, B). In the sixth case the chest lead QRS pattern was normal in the entire series of records and the S–T–T

had returned to normal (figure 3, A). This case, therefore, would be difficult to diagnose once the records were stabilized.

The foregoing analysis indicates clearly that the QRS pattern in which deep S_2 and S_3 are present in diphasic QRS complexes in association with a

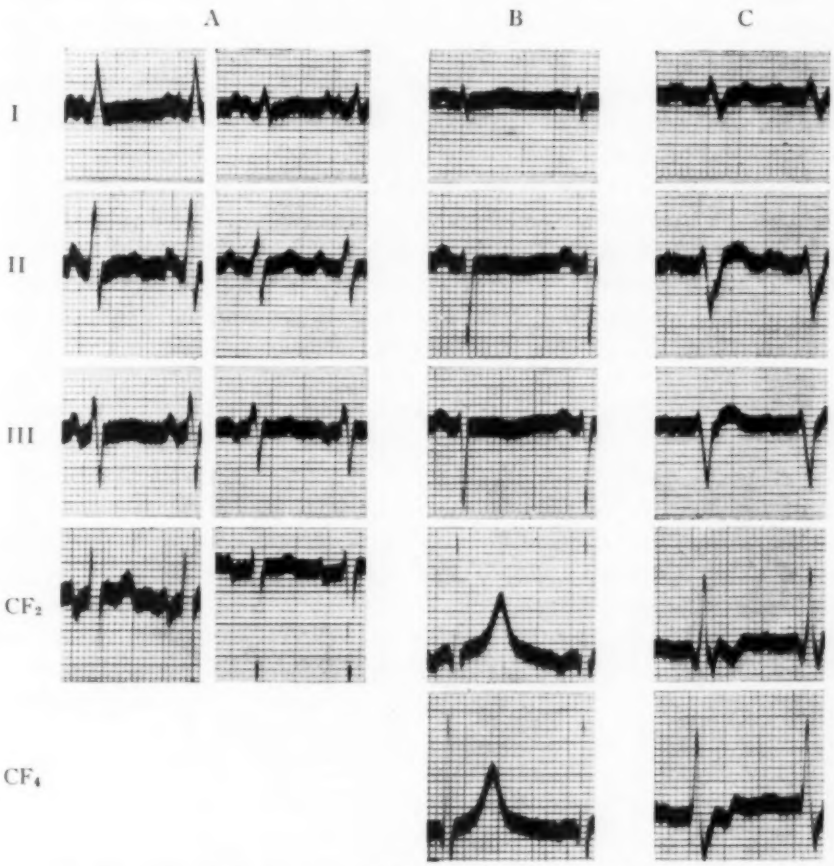

FIG. 4. Three autopsied cases with QRS patterns resembling the type I of anterior wall infarction but due to other conditions. In these cases there is an absence of findings indicative of infarction in the chest leads and QRS, is of the S type. Discussed in text.

A is a case of multiple valvulitis (rheumatic) leading to bilateral ventricular hypertrophy. Note the broad notched P waves in Lead I. The two records were taken 11 days apart.

B is a case of bilateral ventricular hypertrophy with marked emphysema to account for the right heart strain. There was nothing in the clinical story or autopsy protocol to explain the strain on the left heart.

C is a case of severe coronary sclerosis and myocardial fibrosis and the resulting bilateral ventricular hypertrophy. No evidence of myocardial infarction (old or recent) was seen. Note that the electrocardiogram shows evidence of intraventricular block (QRS longer than 0.12 sec.).

relatively small QRS in Lead I (smaller than either S_2 or S_3) may be the residue of an anterior wall infarction whether left ventricular hypertrophy is present or not. Furthermore, while the QRST pattern in the chest leads

may remain characteristic of the old anterior wall infarction, occasionally even this is absent.

1. *Other Causes for the QRS Pattern Resembling Type I QRS of Anterior Wall Infarction and Their Differentiation.* In order to determine under what other circumstances a QRS pattern in the limb leads resembling this type occurred, a survey was made for serial curves in our files showing this pattern (figure 4). Eleven cases selected at random were found in which this pattern occurred without S–T–T changes pointing to anterior wall infarction and in which the clinical history and findings or the autopsy showed the absence of infarction.

Seven of these 11 cases had necropsies and six of these showed evidence of combined left and right ventricular strain leading to measurable hypertrophy of both ventricles. The cause of the combined left and right strain was due in two instances to old rheumatic heart disease with multiple valvulitis (in one there was involvement of the aortic, mitral, and tricuspid valves and in the other, involvement of the latter two valves) (figure 4, A). In two other instances there was chronic cor pulmonale associated with emphysema, both of these patients having had bronchial asthma; the hypertrophy of the left ventricle in one of these was caused by systemic hypertension evident clinically, in the other, its cause could not be determined (figure 4, B). In all of the above four cases the coronary arteries were normal at necropsy. The only two of the seven autopsied cases showing intraventricular block revealed severe coronary artery disease and myocardial fibrosis, in addition to the hypertrophy of both ventricles (figure 4, C). No cause for the hypertrophy was revealed other than the severe coronary sclerosis and this was considered its cause.[12] The last of the seven autopsied cases showed moderate coronary sclerosis with moderate myocardial fibrosis and "brown atrophy" but no valvular deformities or measurable hypertrophy. The roentgenogram and autopsy both revealed a very low diaphragm and dropped heart, and the QRS pattern was explained on this basis (discussed below).

In three of the other four cases without autopsy, pulmonary emphysema was present, associated in one instance with mild hypertension and in the other two with evidence of marked arteriosclerotic heart disease. In the fourth case there was no clinical evidence of heart disease or any cardiac history, the records on this 44 year old patient being taken as a check before electric shock therapy for his mental state.

The differentiation of these cases from the type I QRS pattern of anterior wall infarction is not too difficult. Aside from the absence of the S–T–T changes characteristic of anterior wall infarction, none of these cases had a Q_1 type pattern whereas 19 of the 35 cases with infarction did. Furthermore, the chest lead QRST patterns were not indicative of either recent or old anterior wall infarction. The chest lead QRS patterns in four of these were within normal limits while the other six showed a QRS in lead CF_2 that was abnormal in being upright and W-shaped (figure 4, B and C) with an initial inverted phase less than 3 mm.; this was associated with the same type of

QRS in lead CF_4 (normal in this lead) in some (figure 4, B). In only two of the 11 cases was QRS in CF_2 mainly inverted, but here the first upright phase was more than two millimeters and thus fell within the normal range; in these two cases the QRS in lead CF_4 was normal, being upright and W-shaped. The eleventh case had no chest leads.

The cause of this peculiar QRS pattern in the absence of infarction appears to be due to combined heart strain, the change in QRS_1 being due to right ventricular strain, and the changes in QRS_2 and QRS_3 to left ventricular strain. It is significant that this pattern is seen relatively more frequently in cases of chronic cor pulmonale associated with left heart strain than in cases of combined heart strain due to rheumatic heart disease. This difference may be due in part to the change in the heart's position in association with the low diaphragm, viz., a more pendulous heart with rotation on its own long axis from right to left. Cases have been reported [13] in which this QRS pattern occurred with a low diaphragm and pendulous heart without clinical evidence of either right or left heart strain; this was present in one of our own cases. The cause of this QRS pattern, aside from anterior wall infarction, therefore, appears to be either combined heart strain (figure 4, A and B), a pendulous heart, or both in combination. In addition, this pattern occurring with intraventricular block as in two of our cases of combined strain (figure 4, C) may be due not only to the above causes, but possibly also to bilateral involvement of the bundle branch systems or to unilateral block in one of the bundle branch systems with muscular hypertrophy of the contralateral ventricle. The type I QRS pattern has also been described as a transitory change occurring in anginal attacks.[14]

Thus, there are a number of factors in addition to anterior wall infarction which give rise to this QRS pattern, but the occurrence of a relatively small QRS_1 and diphasic QRS with deep S waves in Leads II and III should always arouse suspicion of an anterior wall infarction, and this cause should be excluded before attributing it to other mechanisms. In this regard, the S–T–T pattern and evolution, the presence or absence of a Q_1 type pattern, and the QRST pattern of the chest leads are valuable adjuncts in the differentiation.

2. *Cause for the Type I QRS Pattern in Anterior Wall Infarction.* Obviously this QRS pattern may have existed before the infarction occurred and its cause would thus be the same as in cases without infarction. It could furthermore be due to infarction superimposed on a preëxisting left ventricular preponderance, several examples of which have been cited above (four out of six cases with control records), or on a preëxisting intraventricular block of which no examples could be found in our series, since none of the six cases with control records had intraventricular block before the infarction occurred.

A clue to another cause of this pattern is revealed by the great frequency of intraventricular block occurring in this type (figure 5), viz., 13 out of 35 cases (37 per cent) as compared with 18 out of 159 cases (11 per cent) in all other QRS patterns, or 31 out of all 194 patterns (16 per cent). The chest

lead QRS pattern in these 13 cases with intraventricular block is of the variety seen with intraventricular block of the broad S_1 pattern occurring with anterior wall infarction and attributable to involvement of the right bundle branch system.[15] It would appear that block involving the right

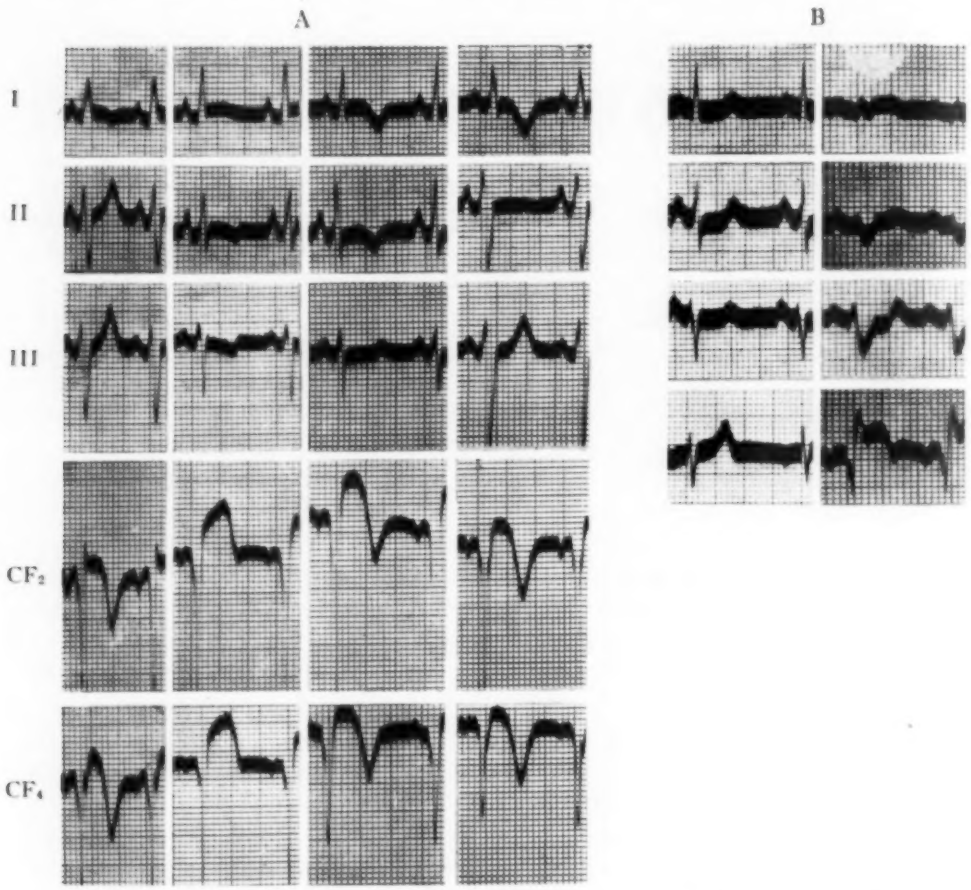

FIG. 5. Two cases of anterior wall infarction to show the influence of intraventricular block in producing the type I QRS pattern. Discussed in text.

A. The series of records was taken 2, 5, 15 and 31 days after the development of infarction. This is an instance of intermittent intraventricular block; the block (with QRS longer than 0.11 second) present in the first and fourth records and absent in the second and third. In this case, only when intraventricular block developed did the characteristic type I QRS pattern appear. Note the characteristic chest leads.

B. A control record and a record taken two days after the development of the infarction. After infarction, intraventricular block developed with a characteristic type I QRS pattern. The chest lead CF_2 is also characteristic and shows the diphasic Q type pattern.

bundle branch system due to infarction of the septum as well as of the anterior wall was responsible for this combination. In three of the cases with intraventricular block in which autopsy findings were available, such septal and anterior wall infarction was found, the septum being involved in

the region adjacent to the anterior wall. The relationship of this pattern to QRS prolongation is further shown by the fact that in five cases this pattern developed only when QRS lengthened to 0.10 second or more in duration, even though the electrocardiogram before this time had already assumed a characteristic coronary contour as evidenced by the S–T–T changes. Furthermore, in three of these five cases, this QRS pattern was only a transitory finding, disappearing when QRS again became shorter in duration (figure 5, A). Even in those cases not showing sufficient QRS prolongation to merit the diagnosis of intraventricular block, this type I QRS pattern may be due to extension of the infarct to the interventricular septum, as occurred in six of the nine autopsied cases showing a QRS of not more than 0.12 second in duration.

Thus it would appear that this QRS pattern in anterior wall infarction may be due to (*a*) causes giving rise to this pattern in the absence of infarction, (*b*) to the superimposition of an anterior wall infarction on a preexisting left ventricular preponderance, (*c*) to the superimposition of anterior wall infarction on preëxisting intraventricular block (of the right bundle branch system) from any cause, (*d*) to the simultaneous or successive involvement of the anterior wall and adjacent septum by the infarct, or (*e*) to infarction of the anterior wall alone.

3. *Prognostic Significance of the Type I QRS Pattern in Anterior Wall Infarction.* It was not possible to make a satisfactory follow-up on these cases of infarction so as to compile accurate mortality figures. We were, however, able to determine which had autopsies at the hospital. It is significant that 12 of the 35 cases of the type I QRS pattern (⅓) had necropsies, whereas only 12 of the remaining 155 cases (1/13) had necropsies. Thus, it appears that cases of anterior wall infarction showing the type I QRS pattern have a poorer life expectancy than those showing other patterns. Apparently they represent instances of more extensive infarction or the superimposition of infarction on an already severely damaged heart whatever its cause.

B. Type II QRS Pattern of Anterior Wall Infarction. Since both the decrease in size of QRS_1 and the development of deep S_2 and S_3 were demonstrated to occur after infarction in type I, it is obvious that either of the above changes might occur without the other.

In the type II series, 28 cases of infarction with diphasic QRS complexes in Leads II and III with deep S waves in both and without a small QRS_1 (figure 6) were found (type 2, table 3). In all of these, except when low "voltage" was present, QRS_1 was more than 5 mm. in height, and in none was the S_2 as large as the upright phase of QRS_1. It is noteworthy that none of these cases came to necropsy, indicating a better life expectancy than in the group with type I QRS pattern. In five of these there was a Q_1 pattern; in the other 23, the only change in the QRS pattern in the limb leads (excluding intraventricular block and low "voltage") was the presence of deep S_2

and S_3. The problem of differential diagnosis from left ventricular preponderance once the records became stabilized is more difficult than in the cases of type I.

In three cases without control records, the S waves in Leads II and III were seen to become deeper during the early evolution of the series. In four cases out of five in which control records were available, the S waves were seen to develop after the infarction occurred. In two of these, QRS was upright in all three limb leads in the control records (figure 6, A); in the third, there was a small S wave in Lead II and a definite Q wave in Lead III in the control; and in the fourth definite Q waves in Leads II and III were present in the control record, the residue of an old posterior wall infarct. In all of these, therefore, the S waves in Leads II and III were clearly due to the anterior wall infarction alone. The case with the Q_2 and Q_3 pattern in the control also developed intraventricular block after infarction occurred (figure 6, C). The fifth case with a control record showed the first type of left ventricular preponderance in the control, and after infarction occurred the S_2 and S_3 became more pronounced.

It would appear, therefore, that whereas the type II QRS pattern of anterior wall infarction may be evidence of a preëxisting left ventricular preponderance or intraventricular block, it may, on the other hand, be the sole QRS contour change, with or without intraventricular block, in some cases of anterior wall infarction. It need not be associated with a Q_1 type and may remain as the sole residue of an old anterior wall infarct (figure 6, B). Therefore, cases showing as their sole abnormality deep S waves in Leads II and III are not always indicative of left ventricular preponderance, but may, on occasion, represent the only evidence of an old anterior wall infarction in the absence of left ventricular strain or hypertrophy.

FIG. 6. Three cases of anterior wall infarction showing the development of the type II QRS pattern after infarction, viz., S_2 and S_3 with S_2 *not* larger in amplitude than QRS_1. Discussed in text.

A. The series shows a control record before infarction and records taken seven days, nine days and one month after a recent myocardial infarction. Note the appearance of a deep S_2 and S_3 without a decrease in amplitude of QRS_1 which, in the last record, makes the curve resemble that of left ventricular preponderance. However, the chest leads are characteristic and even in the last record would indicate the correct etiology of the QRS pattern of the limb leads.

B. The series shows records taken one day, three days and five weeks after a recent myocardial infarction. Note that while QRS_1 became smaller in the second and third records, the S_2 that developed was not larger than the amplitude of QRS_1. The first record shows the S–T–T changes in the limb leads seen in the earliest stage of infarction. The second record is diagnostic including the S–T–T pattern although the chest leads are not except for QRS in CF_2 (already present in the first record). The third record, taken a month later, resembles the contour of left ventricular preponderance and there is nothing at this time to point to infarction as its cause.

C. The first record taken 10 days after a recent myocardial infarction has a QRS pattern of posterior wall infarction in the limb leads, while the S–T–T in the limb leads and both QRS and S–T–T in the chest leads are typical of anterior wall infarction. The second record was taken one year later, and in the interim there was a questionable history of another infarction. This record shows intraventricular block (QRS longer than 0.12 second) and with this block the type II QRS pattern of anterior wall infarction developed. While QRS_1 is decreased in size it is still larger than the S_2 which distinguishes the type II from the type I pattern.

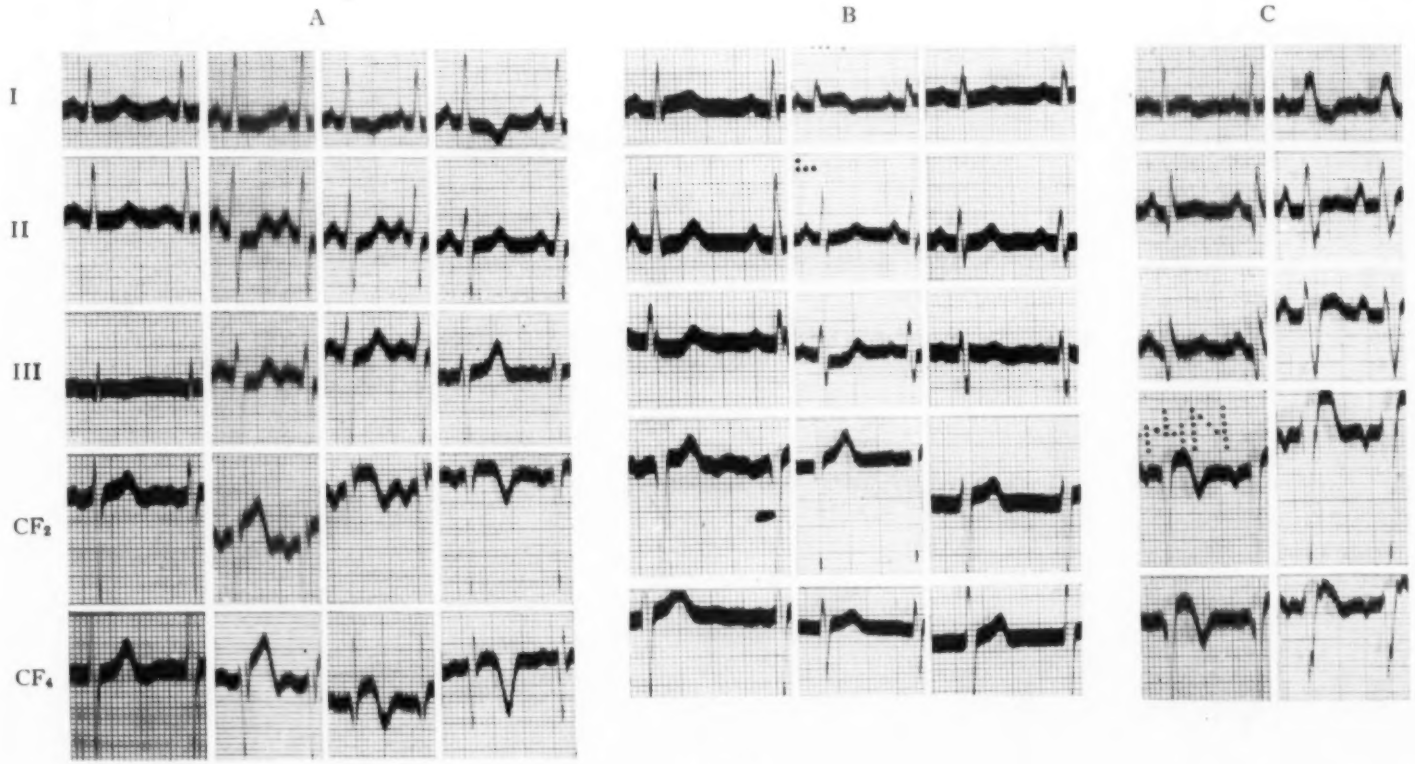

FIG. 6.

The presence of S_2 and S_3 in anterior wall infarction gives the mirror image of the Q_2 and Q_3 pattern seen so frequently in posterior wall infarction, and suggests that the diametrically opposite location of the infarcts gives rise to these mirror image changes. In addition to emphasizing changes in QRS_1 in anterior wall infarction, the occurrence of deep S_2 and S_3 deserves stress. The demonstrable occurrence of S_2 and S_3 alone in anterior wall infarction in the absence of left ventricular strain has led us to avoid the latter diagnosis in the presence of anterior wall infarction without other substantiating evidence for its presence.

C. Type III QRS Pattern of Anterior Wall Infarction. In this series 15 cases of small, mainly upright QRS_1 without deep S_2 and S_3 were found (type III, table 3), showing that this may be the sole limb lead QRS change in anterior wall infarction. In almost one-half of these (seven cases) a Q_1 pattern was encountered.

Whereas the small QRS_1 may be the result of a preëxisting right axis shift, as was true in one case with a control record showing a small QRS_1 with a noticeable S wave, the small QRS_1 is usually the result of the infarction per se. In three of the cases with control records the electrocardiogram showed no QRS abnormalities in the controls, and the QRS_1 was seen to decrease in size from 12 to 3, from 9 to 3, and from 5 to 1 mm. respectively.

The diagnosis in three of the 15 cases was confirmed at necropsy, and no cardiac enlargement or noticeable displacement was found, the infarcts being the only abnormalities and being extensive in all, involving also the adjacent septum in two instances. Small upright QRS_1 may persist for some time,

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FIG. 7. Four cases of anterior wall infarction showing the development of the type III QRS pattern after infarction in one (A), viz., QRS_1 small without S_2 or S_3 appearing; and of the type IV QRS pattern after infarction in three (B, C and D) viz., QRS_1 becoming mainly or entirely inverted with QRS_2 upright. Discussed in text.

A. The two records were taken, respectively, during the healing stage and about 18 months after a recent myocardial infarction. At the time of the second record the type III QRS pattern had disappeared although the chest leads and the small inverted T_1 were the residue of the infarction. The first record shows the typical maximal T stage, a characteristic QRS in CF_2, and in the limb leads a tiny QRS_1, the type III QRS pattern.

B. The three records were taken one, three and 11 days after the development of infarction. In the first record a small QRS_1 with a Q_1 is the only QRS abnormality in the limb leads making it a type III QRS pattern. In the other two records QRS_1 becomes inverted which, with QRS_2 and QRS_3 upright, makes this a type IV QRS pattern. In the second record QRS_1 is the triphasic W-shaped equivalent of the diphasic Q pattern, and in the third record the QRS_1 is inverted and notched, also an equivalent of the diphasic Q pattern. These characteristics of QRS_1 distinguish it from the inverted QRS_1 seen in right ventricular preponderance and aside from this, the S–T–T pattern and evolution, and the QRS in the chest leads are characteristic of the anterior wall pattern.

C. This record taken during the healing stage of a recent myocardial infarction shows a type IV QRS pattern. While the infarct is responsible for the QRS in the chest leads and the S–T–T configuration, in both limb and chest leads, the presence of deep S waves in Leads I and II as well as the presence of P-pulmonale suggests that the pattern in this record is the result of anterior infarction superimposed on a preëxisting right ventricular preponderance.

D. The first record is a control taken before infarction, and the second was taken 11 days after the development of infarction. In the second record, QRS_1 becomes entirely inverted, the equivalent of the diphasic Q pattern, making this a type IV QRS pattern.

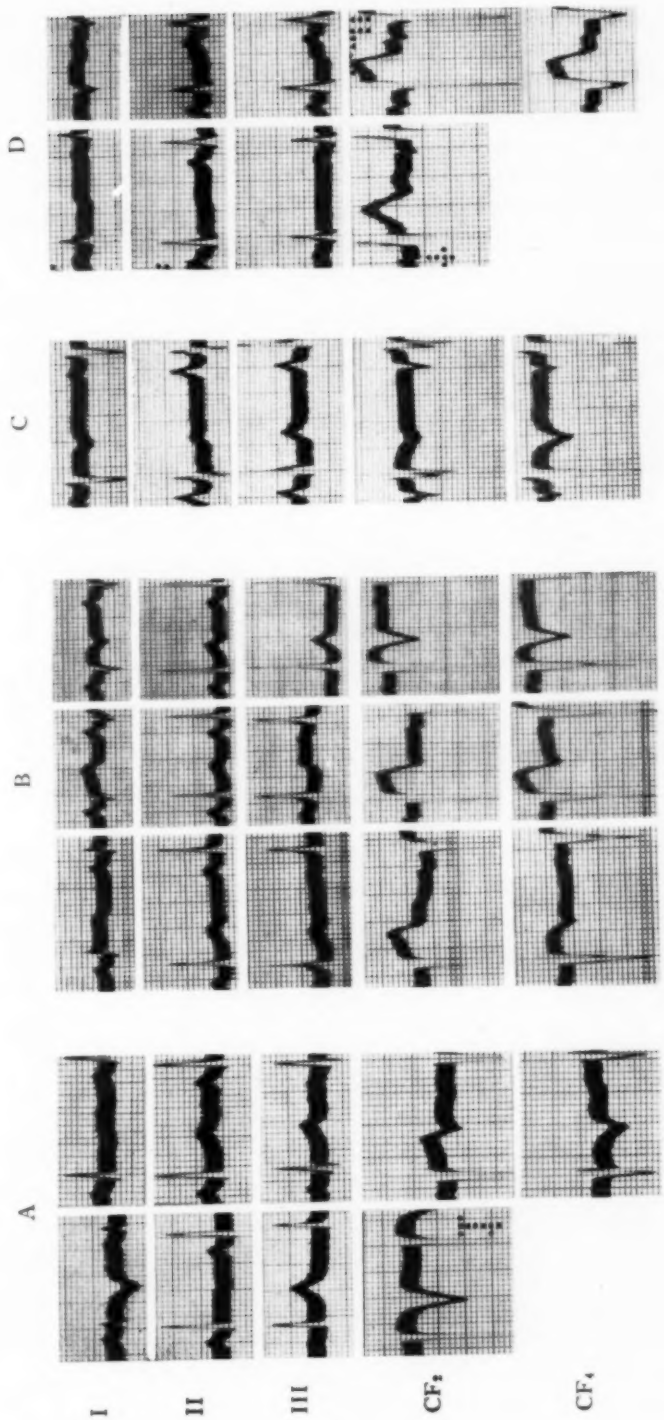

FIG. 7.

and may be the sole QRS pattern residue of an old anterior wall infarct with or without a Q_1 pattern. On the other hand, the QRS_1 may, during the process of restitution, return to its normal size (figure 7, A).

D. Type IV QRS Pattern of Anterior Wall Infarction. In this series 14 cases showed a mainly inverted QRS_1 with an upright QRS_3 (type IV, table 3). One-half of them (seven cases) showed a Q_1 pattern. In four others, QRS_1 was entirely inverted with notching on the downstroke, this being considered a variant of the triphasic Q_1 pattern since all four showed a preceding or succeeding triphasic Q_1 type (figure 7, B). In two other cases, however, QRS_1 was entirely inverted without notching (figure 7, D), and in three others it was associated with a deep S_1. One of the latter had also P-pulmonale (figure 7, C) [16] and gave a history of long standing bronchiectasis and emphysema; the other two cases with S_1 may also have had QRS_1 inversion on the basis of preëxisting right ventricular preponderance. It is, of course, difficult to say whether the two cases with QRS_1 entirely inverted and without notching have the significance of a Q or an S wave, although the former seems more likely. This is substantiated by the fact that one of the cases showing QRS_1 entirely inverted without notching developed this contour only after infarction occurred, and autopsy study of this case revealed no evidence of right ventricular or any other form of cardiac hypertrophy. Another autopsied case showed a mainly inverted triphasic Q_1 type, and here also no cardiac hypertrophy was demonstrable. Three other cases of this type showing the triphasic Q_1 pattern had control records taken before the infarction appeared, and all showed normal, upright QRS_1.

Thus, it would appear that not only the diphasic and triphasic Q_1 patterns are characteristic of anterior wall infarction when QRS_1 is mainly inverted, but that this is true also of the inverted QRS_1 that is notched on the downstroke (figure 7, B) or may even be the case when QRS_1 is inverted and not notched (figure 7, D). These may all, therefore, be considered as equivalents of the Q_1 pattern. In the development of none of these patterns is the presence of right ventricular strain essential as shown by both control records and autopsy studies.[17] None of these QRS_1 patterns should, therefore, be considered as evidence of right ventricular strain in the presence of anterior wall infarction. When, however, a diphasic QRS_1 with a deep S_1 is present, the problem is more complex (figure 7, C). We have no evidence to show that infarction will produce this pattern in the absence of preëxisting right ventricular hypertrophy or, at least, a preëxisting normal right axis shift. Nevertheless, although preëxisting right heart strain must be considered, its diagnosis in the presence of an anterior wall infarction demands other evidence than QRS_1 inversion alone.

E. Type V QRS Pattern of Anterior Wall Infarction. There were only four cases in this group (type V, table 3) in which QRS was mainly or entirely inverted in all three limb leads (figure 8, C and D). In three of the four there was an associated low "voltage." This type with low "voltage"

considered almost pathognomonic of anterior wall infarction by Wintern-itz [61] is thus rare (figure 8, D). In our entire series including all types of infarction only the four foregoing cases were encountered. In one of these, there subsequently developed a superimposed posterior wall infarct pattern, and the limb lead QRS complexes retained their inverted characteristics. No autopsy findings were available in any of these cases.

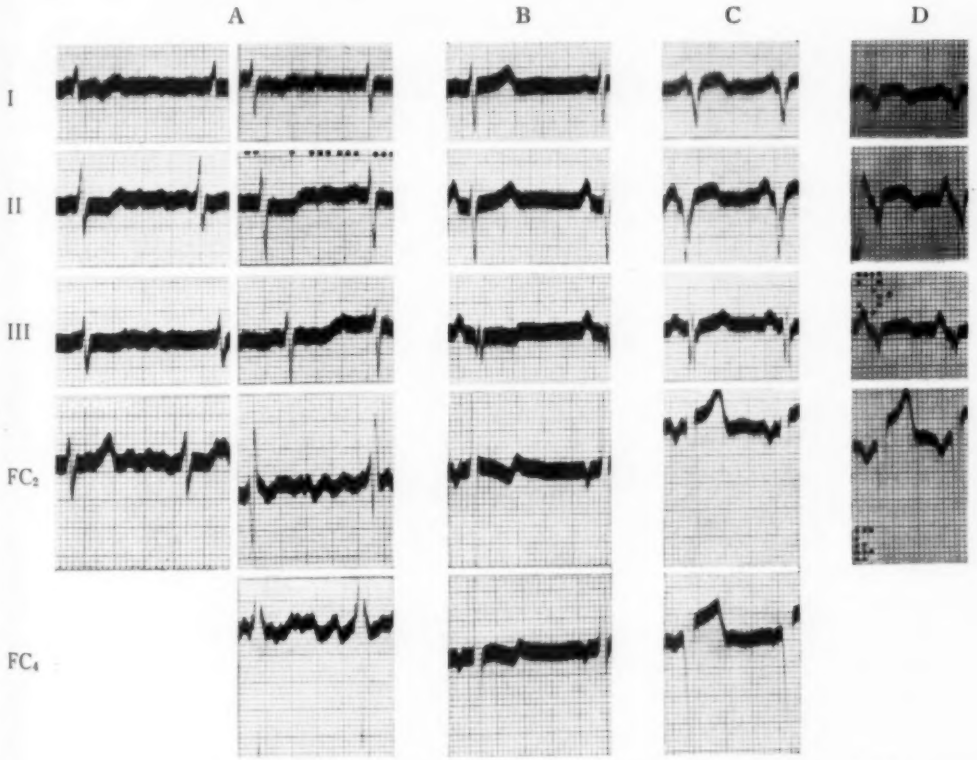

FIG. 8. Two cases of anterior wall infarction (C and D) showing the type V QRS pattern, viz., QRS entirely or chiefly inverted in all the limb leads, and, in addition, two cases of cardiac disease without infarction (A and B) in which a similar QRS pattern is encountered. (Discussed in text.)

A. The two records taken five years apart show the development of mainly inverted QRS complexes in the limb leads in the second record. This is a case of rheumatic heart disease with combined right and left ventricular strain due to a combination of mitral and aortic valvular deformity. Note the presence of deep S waves in the limb leads, and abnormal chest leads in the second record. Both records show auricular fibrillation.

B. From a case of congenital heart disease in a 58 year old man. The chest leads are abnormal but do not indicate infarction. Note the presence of deep S-waves in Leads I and II.

C. Record was taken eight months after a typical clinical attack of myocardial infarction. In addition to having QRS_1 and QRS_2 entirely inverted (the equivalent of the diphasic Q pattern) the QRS configuration in the chest leads is characteristic also. These QRS changes (type V QRS pattern) are the residue of the anterior wall infarction.

D. Record was taken three days after the development of myocardial infarction. Besides low "voltage," characteristic chest lead and S–T–T configuration, the QRS complexes in the limb leads are entirely inverted and notched (the equivalent of the diphasic Q pattern) and constitute the type V QRS pattern of anterior wall infarction.

Inverted QRS in all three limb leads occurs in circumstances other than anterior wall infarction. In our files it was encountered in congenital heart disease (figure 8, B) and in combined right and left heart strain (figure 8, A). In the cases not due to an anterior wall infarct there are, as a rule, S waves in Leads I and II or in all three limb leads, and, most important, the QRS is of normal "voltage," often being unusually large in cases of congenital heart disease. In the cases due to anterior wall infarction, a Q_1 pattern or QRS_1 entirely inverted is seen (figure 8, C and D). QRS_2 in these cases shows the same configuration as QRS_1. In three of the four cases, QRS_3 was W-shaped (figure 8, C) and in the fourth M-shaped. The presence of this QRS contour in Lead III suggests that the type V QRS pattern is actually indicative of extensive involvement extending to the lateral and posterior walls of the left ventricle, or may even indicate the presence of more than one infarct.[18]

F. Conclusions Concerning QRS Patterns in Anterior Wall Infarction. No one limb lead QRS pattern is found consistently in anterior wall infarction. In fact, in 83 cases neither a Q_1 type nor any of the five other types described was present. Low "voltage" occurred in only one-sixth of the cases, the Q_1 type in a little more than one-fourth of the cases, and intraventricular block in one-sixth of the cases. Aside from the characteristic Q_1 type, the other diagnostic types are the type I QRS pattern which occurs in a little more than one-fifth of the cases and the type V QRS pattern with low "voltage" which is rare (three cases). Other circumstances not related to infarction may give QRS patterns like types I and V. The differentiation is made on the basis of the S–T–T contour in the limb leads, the presence or absence of the Q_1 type, and the QRST configuration in the chest leads and their evolution. The appearance of limb lead QRS contours resembling right, left, and combined heart strain in anterior wall infarction indicates the need of caution in ascribing the contour to heart strain in the

FIG. 9. Three cases of anterior wall infarction showing complete restitution except for a residue in the characteristic QRS of the chest leads. Discussed in text.

A. The first record is the control before infarction. The second and third records were taken two days and six months after the development of infarction. The second record is characteristic of anterior wall infarction in all 5 leads and shows, in addition, a small QRS_1 with QRS_2 and QRS_3 upright (type III QRS pattern); QRS_1 is triphasic (W-shaped), the equivalent of the diphasic Q pattern. In the third record all the characteristic QRS and S–T–T contours have disappeared except for the QRS in CF_2 which is entirely inverted and notched on its downstroke.

B. The two records were taken three and one-half months apart, the first during the healing stage of a myocardial infarction. In the first record the S–T–T in the limb leads is characteristic of anterior wall infarction as are the S–T–T and QRS of the chest leads. In the second record all these contours have disappeared except for the QRS in CF_2 and diphasic T in CF_2 and CF_4.

C. The two records were taken 22 months apart, the first during the healing stage of a myocardial infarction. In the first record the five leads are characteristic of anterior wall infarction, the QRS pattern in the limb leads being intermediate between the type I and type II QRS pattern and QRS_1 being the triphasic W-shaped equivalent of the diphasic Q type. In the second record all these characteristics have disappeared, the record being the sort seen in the mixed type of left ventricular preponderance even including the almost entirely inverted QRS in CF_2 which is often found in left preponderance in the absence of infarction.

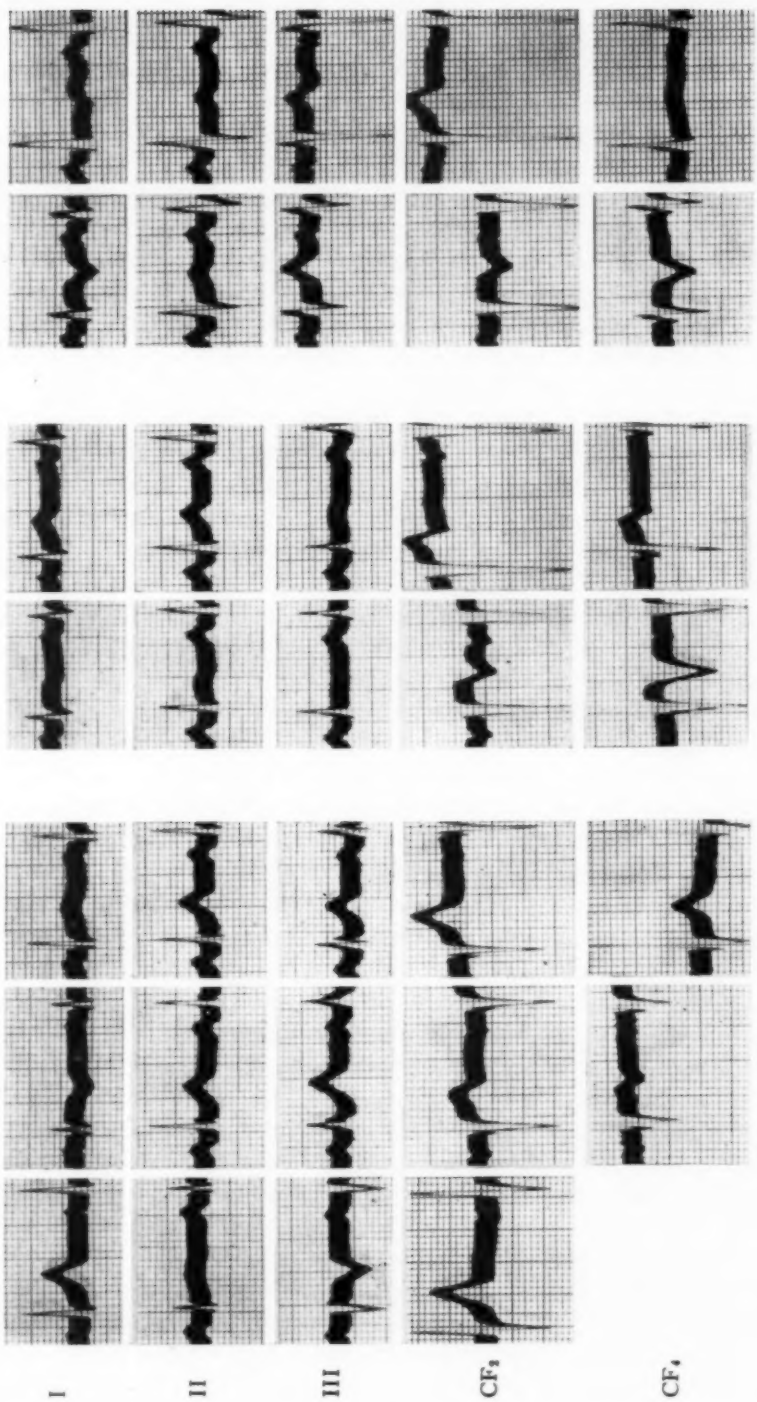

FIG. 9.

presence of infarction, since the evidence presented has indicated that infarction per se may give these patterns. Furthermore, it has been shown in this study that some of the cases showing limb lead QRS changes pointing to these varieties of ventricular strain may be the residue of old anterior wall infarction. The differentiation in such instances is aided by the configuration of the S–T–T complexes in the limb leads, the QRS_1 contour, and the entire ventricular complex in the chest leads, any or all of which may show changes not expected in ventricular preponderance but encountered in stabilized records of old infarction. The changes of the S–T–T segment in the limb leads are familiar, but those in the chest leads merit mention. They consist of T inversion in CF_2 or in CF_2 and CF_4 associated with an upward bowed S–T segment elevated above the isoelectric level (figures 5, A and 7, B).

G. Chest Lead QRS Patterns in Anterior Wall Infarction. In only 5 per cent of all the cases of anterior wall infarction were normal QRS complexes encountered in the chest leads (figure 3, A). In the remaining 95 per cent, QRS was abnormal. The abnormalities consisted of (*a*) entirely inverted QRS (figure 7, B), (*b*) entirely inverted QRS with a marked notching on the downstroke (figure 9, A and B), (*c*) diphasic or triphasic QRS with an initial inverted phase of more than 3 mm. (figures 2, A, 3, B, 5, B), and (*d*) almost entirely inverted QRS of the diphasic variety with the first phase upward but less than 2 mm. in height (figures 2, B, 7, C). The forms (*a*), (*b*), and (*c*) are more characteristic [19] than (*d*), since the latter is encountered also in left ventricular preponderance (figure 9, C), intraventricular block, and in other circumstances besides anterior wall infarction, especially when only lead CF_2 is involved. It is essential, therefore, that the contour of the QRST be observed as a unit in order to differentiate other conditions from anterior wall infarction.

In the 143 cases having both leads CF_2 and CF_4, 81 showed QRS entirely or almost entirely inverted in both leads, 31 showed this abnormality in lead CF_2 only with lead CF_4 normal, 19 showed the diphasic or triphasic (W) QRS contour with a deeply inverted initial phase, 10 showed no abnormalities of QRS in either lead (although in seven of these the S–T–T was diagnostic of anterior wall infarction), and only two showed a normal QRS in lead CF_2 with an abnormal QRS in lead CF_4. In the 51 cases in which lead CF_2 was the only chest lead taken, 41 had entirely or almost entirely inverted QRS complexes and 10 had diphasic or triphasic (W) QRS complexes with the initial phase deeply inverted. Thus, it is apparent that as far as QRS is concerned, lead CF_2 is far more valuable than lead CF_4 in the diagnosis of anterior wall infarction (figures 2, B, 6, B, 9, A).

The diagnostic value of the chest leads as compared to that of the limb leads is shown further by the fact that in 17 of the 190 cases (9 per cent) of anterior wall infarction, the limb leads showed no specific change in the QRS or S–T–T complexes while the chest leads were pathognomonic; and in only three of the 190 cases (1.5 per cent) were the chest leads normal when

both the QRS and S–T–T were observed, and the diagnosis apparent only in the limb leads.

Summary and Conclusions

1. In an endeavor to increase the diagnostic value of the electrocardiogram, the QRS patterns of 369 series of records with chest leads from cases of definite myocardial infarction were classified.

2. This series included 18 cases of atypical infarction patterns, 20 cases of combined anterior and posterior wall infarction, 141 cases of posterior wall infarction, and 190 cases of anterior wall infarction.

3. Acute diffuse pericarditis complicating infarction was diagnosed in the electrocardiogram in 13 cases; and 41 cases of concordant T-wave inversion in the limb leads (T_N) were encountered.

4. Ninety per cent of the 141 cases of posterior wall infarction showed a Q_3 (or Q_2 and Q_3) or its equivalent. It was concluded that an entirely inverted QRS_3 was equivalent to a Q_3 in the presence of a Q_2 (either a diphasic QRS_2 or a triphasic W-shaped QRS_2 with a deeply inverted initial phase).

5. Only 28 per cent of the 190 cases of anterior wall infarction showed a Q_1 pattern, either with a diphasic or triphasic QRS in this lead. It was concluded that an entirely inverted QRS_1, when notched on the downstroke, was equivalent to a Q_1.

6. The QRS patterns encountered in anterior wall infarction could be grouped into five categories besides a miscellaneous group. These are described.

7. The two most common QRS contours encountered in anterior wall infarction were (*a*) the small upright QRS_1 (or inverted QRS_1) and (*b*) the diphasic QRS_2 and QRS_3 with deep S waves. At times each occurred alone without the other; often they occurred together. Thus a small upright or inverted QRS_1 was encountered in 64 of the 190 cases, and diphasic QRS_2 and QRS_3 with deep S_2 and S_3 were encountered in 63 of the 190 cases.

8. These QRS contours in the limb leads can be caused by the anterior wall infarct per se. This was indicated in cases with control records before infarction and in cases checked by necropsy. The occurrence of these QRS contours in the presence of anterior wall infarction, therefore, does not indicate respectively either right ventricular preponderance when QRS_1 is inverted or left preponderance when S_2 and S_3 are present. In such cases these diagnoses should be avoided even though it appears that deep S_2 and S_3 are more apt to be present in cases with preëxisting left ventricular hypertrophy.

9. The combination of a small upright QRS_1 with deep S_2 and S_3, in which QRS_1 was not so large as S_2, was considered especially significant. It constituted the type I QRS pattern of anterior wall infarction and occurred in 35 of the 190 cases. A large number of these cases had intraventricular block (37 per cent as compared to 16 per cent of the entire group of 190

cases). Septal involvement seemed to be responsible for this QRS pattern in some cases, especially since the pattern developed concomitantly with QRS prolongation and disappeared when the QRS duration returned to normal.

10. The presence of deep S_2 and S_3 with QRS_1 of normal amplitude or, at least, larger than S_2 constituted the type II QRS pattern of anterior wall infarction. It occurred in 28 of the 190 cases.

11. In the stabilized stage in both type I and type II QRS patterns, the QRS contour may be the only residue of the old anterior wall infarction. The differentiation of these cases from left ventricular preponderance, aside from the relatively small QRS_1 in the type I pattern, may be difficult or impossible unless some of the characteristic S–T–T changes remain or unless chest leads are taken. Usually, but not always, there is sufficient evidence in the chest leads to warrant the differentiation between left ventricular hypertrophy and an old anterior wall infarction. This is especially important in cases with the type II pattern. In instances showing the type I QRS pattern as a residue, the small size of the QRS_1 should be sufficient to make one consider the existence of some other lesion than an uncomplicated left ventricular hypertrophy.

12. Eleven cases without infarction were encountered (seven with autopsy confirmation) in which a limb lead QRS pattern similar to that of the type I of anterior wall infarction was seen. In these cases the QRS pattern was attributable to combined right and left ventricular strain, alteration in position of the heart, or to a combination of the two. In these cases neither the chest leads nor the S–T–T configuration of the limb leads showed any of the characteristics seen in anterior wall infarction patterns.

13. A small QRS_1 without deep S_2 and S_3 was seen in 15 of the 190 cases of anterior wall infarction. This constituted the type III QRS pattern.

14. A mainly inverted QRS_1 with QRS_3 upright was seen in 14 of the 190 cases of anterior wall infarction. This constituted the type IV QRS pattern and had to be differentiated from right ventricular preponderance on the basis of the limb lead S–T–T pattern, the contour of the QRS and S–T–T of the chest leads, and the presence or absence of a Q_1.

15. An entirely or chiefly inverted QRS in all three limb leads was encountered only four times in the 190 cases of anterior wall infarction. This constituted the type V QRS pattern. In three cases it was considered pathognomonic of the infarction because it was associated with low "voltage." Cases of QRS inversion in the limb leads were encountered in the absence of anterior wall infarction, e.g., in congenital heart disease and in combined right and left ventricular hypertrophy. The characteristic S–T–T infarct contour of both the limb and chest leads as well as the presence of a Q_1 or its equivalent and low "voltage" helps in the differential diagnosis.

16. The chest leads were found to be essential in the diagnosis of anterior wall infarction in 9 per cent of cases in which the limb lead pattern was not characteristic. In only 5 per cent of the cases were the chest leads not characteristic of infarction and the limb leads diagnostic. It was found that in

chest leads CF_2 and CF_4 the QRS contours most diagnostic of anterior wall infarction were the diphasic QRS with a deeply inverted initial phase, its equivalent, the triphasic QRS with a deeply inverted initial phase, and the entirely inverted QRS with notching on its downstroke. On the other hand, the QRS which is almost entirely inverted with a small initial upright phase is not pathognomonic since it occurs in other conditions besides myocardial infarction. The value of viewing the entire QRST pattern of the chest leads as a unit in diagnosis is emphasized.

17. It is concluded that the QRS pattern is of value in the differential diagnosis in the electrocardiogram of myocardial infarction, and that in doubtful cases it may point to the true cause of the contour seen in the record. This fact in no way depreciates the value of the S–T–T patterns in the diagnosis of myocardial infarction and the utility of the S–T–T evolution in determining whether the infarct is very recent, healing, almost healed, or old. The information obtained by the S–T–T evolution is not replaced by the QRS patterns since these do not undergo such characteristic changes while the infarct is healing.

Addendum. Attention should be drawn to two communications, bearing on this subject, which appeared while this paper was in press.

The first, a communication from this laboratory (R. Langendorf, M. Hurwitz and L. N. Katz, Brit. Heart Jr., 1943, v, 27), deals in part with the QRS patterns of combined heart strain and supplements the data in this report.

The second, which appeared after our study was completed (S. P. Schwartz and H. Marcus, Am. Rev. Tuberc., 1942, xlvi, 35), reported 15 instances out of 24,200 records in which there was concordant inversion of QRS in the limb leads. Five of these were associated with myocardial infarction, two with congenital heart disease, one with bronchial asthma and bronchiectasis, and seven with chronic pulmonary tuberculosis. Autopsy, obtained in 9 of the 10 cases without myocardial infarction, revealed hypertrophy of the right ventricle in seven cases, the remaining two showed dilatation of the right heart without hypertrophy. These authors stress the rôle of rotation of the heart on its longitudinal axis in causing this peculiar electrocardiographic pattern. Not all their cases fall into the type V QRS pattern of anterior wall infarction described by us; some of the cases illustrated in their paper show a small and diphasic QRS, (with an S-wave) and would fit into our type I QRS pattern.

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MYO-EPITHELIAL HAMARTOMA OF THE GASTRO-INTESTINAL TRACT (CLARKE) *

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THE finding of small masses of aberrant epithelial and muscular tissue in various portions of the gastrointestinal tract is not uncommon. The nomenclature of these nodular growths has varied according to the amount and character of the epithelium and its resemblance to known viscera. Thus the large majority of the ectopic foci have been called aberrant or accessory pancreatic tissue, while other designations include "adenomyoma," "Brunner's adenoma," and "incompletely differentiated accessory pancreas." In 1940 Clarke suggested the term "myo-epithelial hamartoma" as an all-inclusive one, to cover all such nodular masses of developmental origin. This designation seems the most applicable. Twenty-four instances of ectopic tumor-like foci will be presented, illustrating variations in epithelial and muscle components, and justifying the use of the term "myo-epithelial hamartoma."

Literature: Complete reviews of the reported cases of aberrant pancreatic tissue have been recorded by Branch and Gross,[1] Pappi,[2] and most recently by Faust and Mudgett.[3] The latter authors have outlined the incidence and sites of occurrence of the nodules. The most frequently involved parts of the gastrointestinal tract are the duodenum (28.37 per cent), the stomach (25.67 per cent) and the jejunum (17.56 per cent). Since the publication of their review several isolated case reports have appeared. From the available literature, there have been collected nine additional cases in the stomach, three in the duodenum, two in the gall-bladder, two in Meckel's diverticula, and one in the jejunum.[4-20] It should be emphasized at this point that the literature cited above refers distinctly to cases of "aberrant pancreatic tissue." In addition to these reports, Clarke [21] added eight instances including four gastric masses, and one each in a Meckel's diverticulum, jejunum, duodenum and gall-bladder. He included adenomyoma as well as aberrant pancreatic tissue. Hintzsche [22] identified isolated islands of cells in the duodenal mucosa as of pancreatic origin. He employed Pappenheim's stain on formalin fixed tissue, and claimed to see nuclei, cytoplasmic granules and fibrillation of the basilar cytoplasm identical with that of pancreatic cells.

In addition to the value of careful recording of incidental postmortem findings, certain important features of immediate clinical application have been stressed by various authors. Thus, the nodules occurring in the region of the pylorus have given rise to symptoms of obstruction.[7] Polypoid tumors have been visualized by roentgenogram of the stomach and duodenum.[15] At

* Received for publication July 29, 1942.
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operation the nodules have been mistaken for malignant tumors, and needless radical surgical procedures have been carried out.[6] Ulceration at the surface of a duodenal nodule has been recorded.[8] Symptoms of hypoglycemia have been attributed to a nodule showing abundant circumscribed islet tissue as well as islet cells diffusely scattered throughout the mass.[20] Intussusception of the ileum at the site of a Meckel's diverticulum which bore a mass of aberrant pancreatic tissue at its apex, has been seen.[5]

Of the histological features of note, typical islands of Langerhans have been seen on numerous occasions. Branch and Gross report islet tissue in nine of their 24 cases. In the pyloric masses glandular tissue closely resembling Brunner's glands is not uncommon.

It will be noted that in the cases reported below, masses occurring in the gastrointestinal tract permit of division into two groups. The first shows typical pancreatic tissue. In the second group the aberrant tissue consists of intermingled smooth muscle and epithelial duct structures.

Case Reports

Case 1. M. L., a 69 year old female, presented the picture of thrombosis of the left middle cerebral artery with extensive encephalomalacia. In the pyloric region a large mass 4 by 1.5 cm. was noted involving the deeper layers of the mucosa extending to the subserosa (figure 1). A small amount of smooth muscle, extensive areas of hyalinization, neurofibromatous elements, and a large dilated duct, were prominent features in the mass.

Case 2. H. S., a 62 year old female, suffered from repeated episodes of ascites, and finally succumbed with a terminal picture of cholemia. A small fluctuant yellow mass resembling a dilated lacteal was seen in the submucosa of the duodenum (figure 2). Pancreatic acini, ducts, and hypertrophic islet tissue were seen separating the layers of the duodenum on microscopy.

Case 3. E. S., a 13 year old female, was operated upon because of symptoms and signs of acute appendicitis. Laparotomy revealed a large Meckel's diverticulum. At the base of the diverticulum a heaped-up granular mucosa resembling gastric mucosa was seen. Distal to this, in the subserosal fat tissue, a firm, grayish trabeculated mass was apparent (figure 3). Microscopic examination of the mass revealed dilated ducts, acinar tissue, and typical pancreatic islets of Langerhans.

Case 4. J. H., a 53 year old female, died with a picture of cachexia after a downward course. Carcinoma of the ovary with widespread metastases was found. A firm white mass 2 by 1 cm. was noted at the fundus of the gall-bladder (figure 4). Dilated ducts and smooth muscle fibers were seen separating the bundles of the muscular wall.

Case 5. M. C., a 48 year old colored female, entered with complaints of herpes zoster of the skin of the thorax, and anemia. At autopsy, generalized Hodgkin's disease was found. A mass measuring 0.5 by 0.5 cm. was seen in the submucosa of the jejunum 10 cm. from the ligament of Treitz. On section, the mass resembled normal pancreatic tissue. Microscopically, islet tissue, acini, and ducts containing eosinophilic inspissated secretion were seen. Metaplasia of the acinar to islet tissue was suggested (figure 5).

Case 6. A. T., a white female infant, suffered extensive birth trauma and died in two months with hydrocephalus. A rounded mass 3 mm. in diameter was seen in the region of the pylorus. Microscopically, large ducts were seen which blended with glands showing typical features of Brunner's glands (figure 6). Suggestive acinar

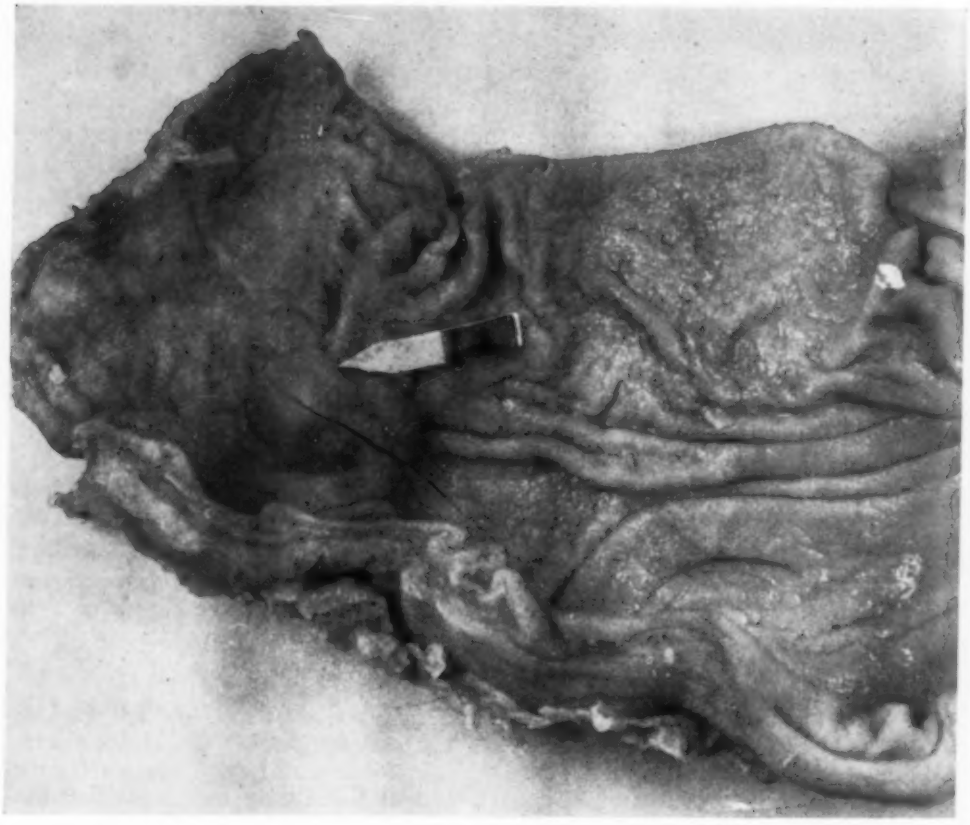

FIG. 1. *Case 1.* Adenomyoma of pylorus extending throughout all layers of gastric wall with some fixation and smoothness to overlying mucosa. Serosal aspect of this mass measured 4 by 1.5 cm. (× 2.)

tissue was noted near the mucosa of the stomach. Xanthomatous areas were seen in the muscularis.

Case 7. L. B., a 64 year old male, died after thyroidectomy, the immediate cause of death being congestive heart failure. A small nodule 0.5 by 0.5 cm. was found in the ileum six inches from the ileocecal valve. The gross diagnosis was leiomyoma. Microscopically, a large amount of smooth muscle was seen, in which were embedded large ducts (figure 7), many containing papillations. No islet tissue was found.

Case 8. F. N., a white female infant, died after nine hours with the clinical picture of hydrops neonatorum. A small nodule was detected in the duodenum ½ cm. above the ampulla. This was composed of dilated duct structures surrounded by muscle.

Case 9. T. C., a 49 year old white female, exhibited the classical symptoms and signs of massive cerebral hemorrhage. In the jejunum 15 cm. from its origin, a mass measuring 2 by 1.5 cm. was seen in the submucosa, extending to the subserosa. Typical elements of pancreatic tissue were seen microscopically, including acini, ducts, and islet tissue.

Case 10. R. R., a 67 year old male, died of hypertensive heart disease with congestive heart failure. A mass 2 by 2 cm. was found in the duodenum 4 cm. from the pylorus. Ducts, acini and a small amount of islet tissue were identified. In some

areas the epithelium of the acini was atrophic and seemed to merge imperceptibly with definite nerve bundles.

Case 11. B. B., a 71 year old male, died of the effects of coronary thrombosis. At autopsy, a firm nodule with cystic zones was seen in the fundus of the gall-bladder. Dilated ducts were noted in the muscular layer, presenting a well circumscribed mass.

FIG. 2. *Case 2.* Nodular submucosal mass of pancreatic tissue in the duodenum. (× 4.)

Case 12. C. S., a 34 year old white female, entered with symptoms of congestive heart failure and died with a diagnosis of malignant nephrosclerosis. In the first part of the duodenum, distinct from the pancreatic head, there was seen a firm mass 2 by 2 cm. Acinar tissue, ducts, and islet tissue were noted in their usual proportion.

Case 13. C. B., a 40 year old white male, was admitted with a fractured tibia, and while on the ward died from a large thrombus of the left coronary artery. A firm mass 1 cm. in diameter was noted at the fundus of the gall-bladder, which on section revealed cystic areas corresponding to dilated duct structures. A small amount of muscle was seen.

Fig. 3.

Fig. 4.

FIG. 3. *Case 3.* Resected Meckel's diverticulum showing triangular mass of differentiated pancreatic tissue at summit of diverticulum in subserosa. Note sharply delimited area of ectopic gastric mucosa below the pancreatic mass. (× 4.)

FIG. 4. *Case 4.* Cystic adenomyoma at fundus of gall-bladder. (× 1.5.)

Case 14. M. W., a 68 year old white female, entered with signs of a generalized peritonitis. At laparotomy a ruptured gall-bladder was found, and the patient died soon after operation. A small mass 0.5 by 0.5 cm. was found at the ampulla of Vater. Microscopically, ducts lined by tall cuboidal epithelium were seen embedded in dense collagenous tissue. The entire ectopic mass was located in the submucosa, and had apparently caused obstruction.

Case 15. T. C., a 55 year old male, was struck by an auto, and died of extensive skull fracture and epidural hematoma. A small nodule in the subserosa of the fundus of the gall-bladder was observed, and contained dilated duct structures mingled with atrophic bundles of smooth muscle.

Case 16. A. C., a 30 year old male, entered the hospital in uremia. At autopsy, large white kidneys of subacute glomerulonephritis were found, in association with subacute bacterial endocarditis. On the posterior wall of the duodenum, above the

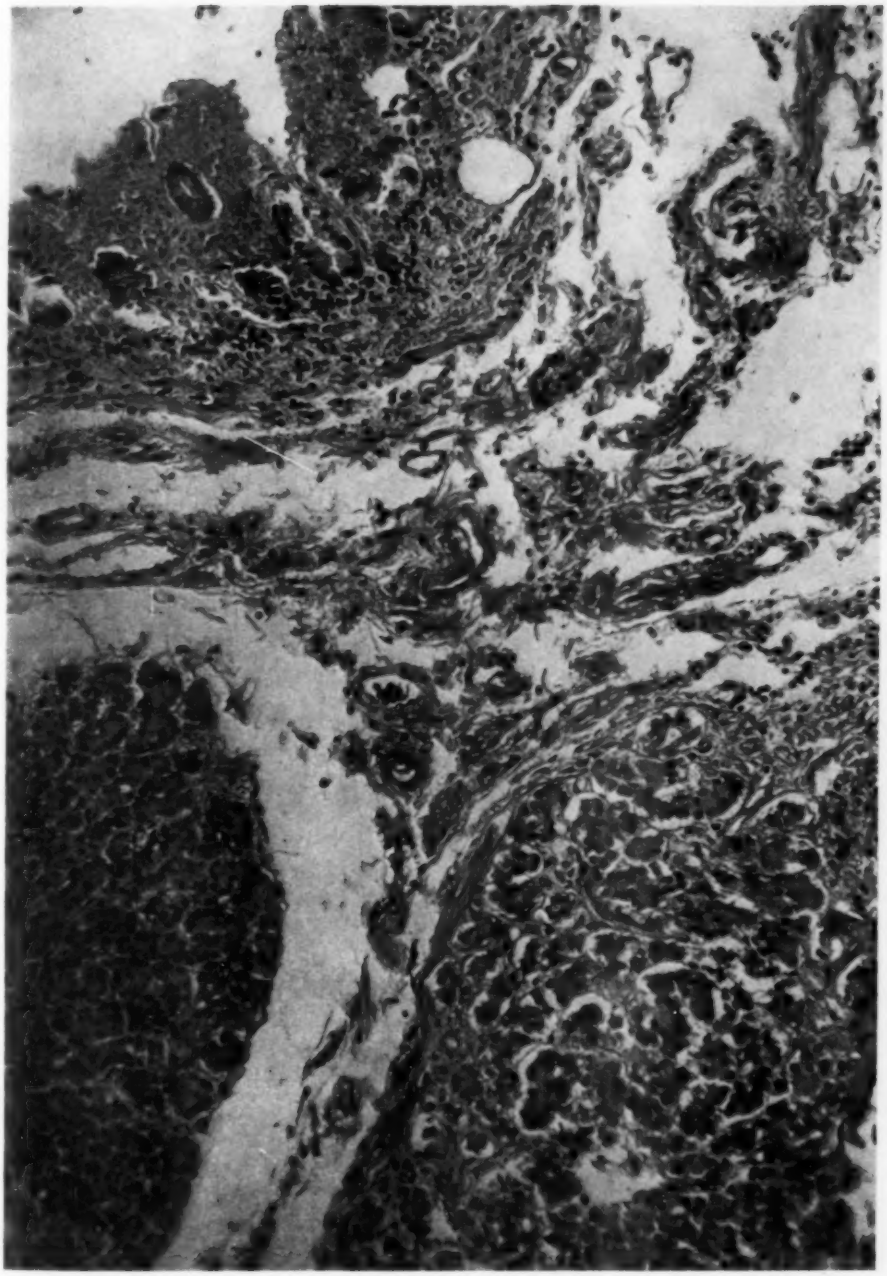

FIG. 5. *Case 5.* Differentiated pancreatic tissue in submucosa of jejunum. Note preserved lobulation. Mucosa and lumen above. (× 175.)

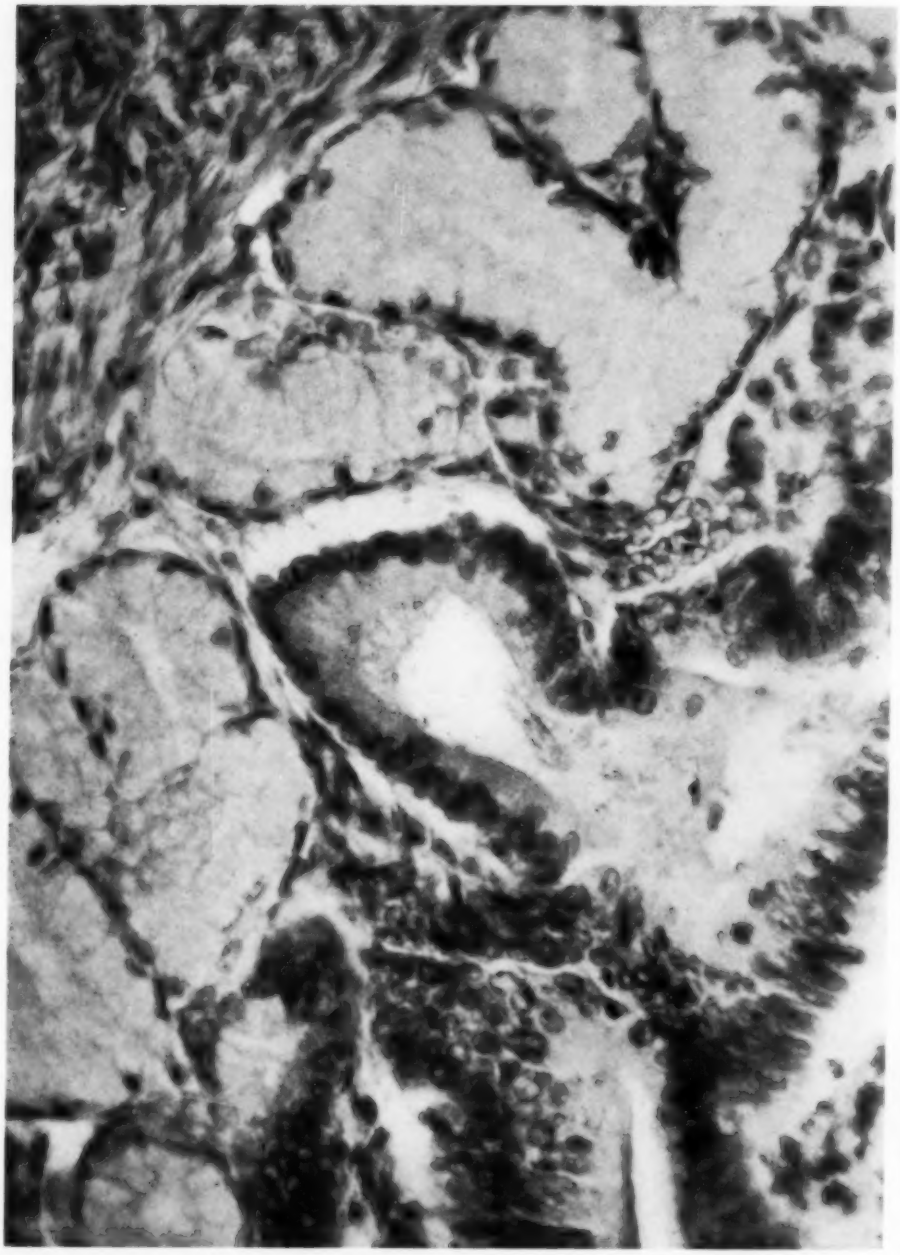

FIG. 6. *Case 6.* Aberrant glandular and muscle tissue with transition from duct structure to Brunner gland-like nests. (× 500.)

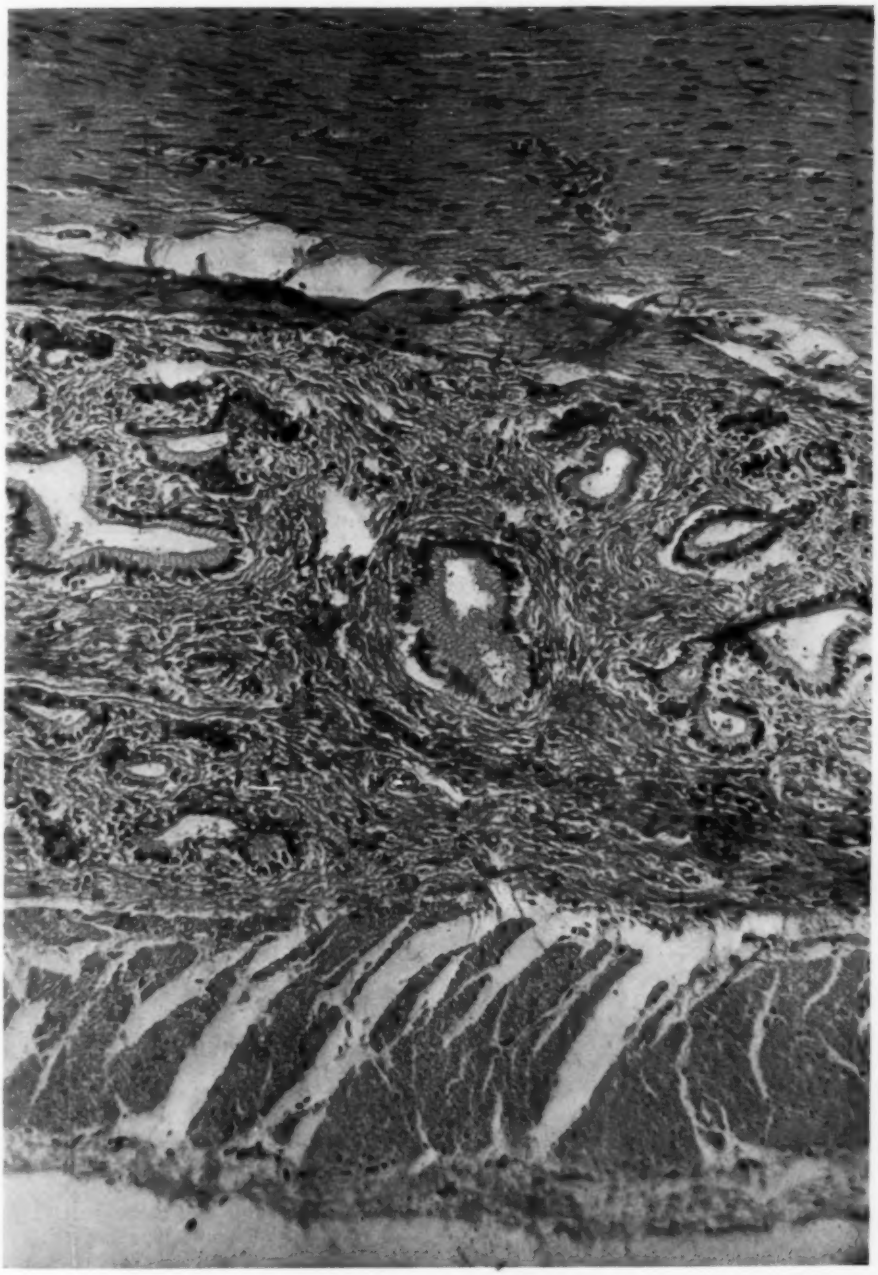

FIG. 7. *Case 7.* Adenomyomatous mass showing marked fibrosis, located between longitudinal and circular muscle planes of wall. Serosa seen below. (× 300.)

ampulla, a small mass 0.5 by 0.5 cm., with overlying ulceration, was seen. Acini and ducts were identified, but no islet tissue was seen.

Case 17. L. S., a 37 year old female, died of extensive tuberculous meningitis. A nodule measuring 1 by .5 cm. was noted in the submucosa of the jejunum. Characteristic pancreatic tissue was seen, with no islet tissue.

Case 18. D. B., a 62 year old male, entered the hospital with severe jaundice, and at autopsy a subacute yellow atrophy of the liver was found. In the fundus of the gall-bladder a mass 0.7 by 0.5 cm. was seen, which contained large ducts enmeshed in thin strands of smooth muscle.

Case 19. T. B., a 62 year old male, died of hypertensive heart with congestive failure. A small cystic mass was found in the subserosa at the fundus of the gall-bladder.

Case 20. C. C., a 53 year old white male, died of chronic myelogenous leukemia after a prolonged downward course. In the proximal portion of the ileum, a small nodule 1 by 0.5 cm. was found in the submucosa. Duct structures with cystic dilatation were seen interspersed among hypertrophied and distorted muscle bundles.

Case 21. A. F., a 45 year old male, died shortly after the onset of severe precordial pain, and showed extensive myocardial infarction at autopsy. A nodule 1 cm. in diameter was found at the pylorus in the submucosa. Microscopically this consisted of acinar tissue and dilated ducts. No islet tissue was seen.

Case 22. M. B., a 62 year old female, died of generalized peritonitis following an attempt at end to end anastomosis of the sigmoid after resection of a perisigmoidal abscess caused by ruptured diverticulitis. A firm nodule 1.5 by 1 cm. was observed at the pylorus. All of the components of normal pancreatic tissue, including islet tissue, were seen.

Case 23. M. W., a 78 year old white female, died shortly after admission for generalized peritonitis due to a ruptured diverticulitis of the sigmoid colon. The fundus of the gall-bladder presented a small mass in the muscularis which revealed dilated duct structures surrounded by a sparse amount of smooth muscle.

Case 24. E. E., a 50 year old colored male, died after a long period of hospitalization, with terminal cachexia due to carcinomatosis. A firm nodule was found in the proximal ileum, measuring 1 by 1 by .5 cm. The mass occupied the submucosa, muscularis and subserosa. Hypertrophic muscle bundles were seen in which were interspersed varying sized ducts, in the largest of which intraductal papillary epithelial proliferation was noted.

Discussion

Division of the 24 cases into two groups is indicated in table 1. The distribution of the aberrant pancreatic tissue conforms closely to that ob-

Table I

Distribution of Gastrointestinal Myo-Epithelial Hamartoma

A. Aberrant Pancreas	11	Pylorus	2	With islet tissue 7
		Duodenum	4	
		Jejunum	2	Without islet tissue 4
		Ileum	2	
		Meckel's diverticulum	1	
B. Adenomyoma	13	Gall-bladder	7	With chronic cholecystitis 1
		Duodenum	1	
		Ampulla of Vater	1	Without chronic cholecystitis 6
		Pylorus	2	
		Ileum	2	

TABLE II

Résumé of 24 Reported Cases

Case No.	Age	Sex	Location	Size	Fibrosis	Islet	Epithelial Components	Muscle Component	Remarks
1	69	F	Pylorus, mucosa, submucosa	0.4 by 1.5	++++	−	Cystic duct structure	Little hyalinization nerve elements extending into mucosa	Inflammation; giant cells
2	62	F	Duodenum, submucosa muscle	0.9 by 0.9	++	+	Acini, ducts	Hypertrophy	Hypertrophy of islets
3	13	F	Meckel's diverticulum, subserosa	1 by 1 by 1	++	+	Acini, ducts with dilatation	—	Ectopic gastric mucosa; operative specimen
4	53	F	Gall-bladder. Fundus muscle	2 by 1	−	−	Ducts (dilated)	Some	Chronic cholecystitis
5	48	F	Jejunum. Submucosa	0.5 by 0.5	−	+	Acini, ducts	—	Inspissated secretion in ducts, metaplasia of acinar to islet tissues
6	2 mo.	F	Pylorus. Submucosa muscle	0.3 by 0.3	−		Ducts, acini (?) Brunner's glands	Xanthoma-like areas	—
7	64	M	Ileum. Submucosa	1.5 by 0.5	+++	−	Acini (atrophic), ducts with papillation	Much hypertrophy	Resembled leiomyoma in gross
8	9 hrs.	F	Duodenum. Submucosa muscle	0.2 by 0.3	−	−	Ducts	Little	—
9	49	F	Jejunum. Subserosa	1.5 by 2	+	+	Acinar tissue, ducts	Little; distortion	Interstitial pancreatitis in aberrant nodule
10	67	M	Duodenum. Submucosa and subserosa	2 by 2	−	+	Acini, ducts	Hypertrophied	Merging of nerve and epithelial tissue (micro.)
11	71	F	Gall-bladder. Fundus	1 by 0.5	−	−	Ducts (cystic)	Little	No cholecystitis
12	34	F	Duodenum. Subserosa	2 by 2	−	+	Acinar tissue, ducts	Distorted; some hypertrophy	—
13	40	M	Gall-bladder. Fundus	1 by 1	+	−	Ducts with some cystic dilatation	Little	No cholecystitis
14	68	F	Duodenum. Submucosa	0.5 by 0.5	++++		Ducts	Hypertrophy; some distortion	Empyema of gall-bladder with peritonitis
15	55	M	Gall-bladder. Fundus submucosa	0.5 by 0.5			No sections	—	No cholecystitis
16	30	M	Duodenum. Submucosa	0.5 by 0.5	+++		Acini, ducts	—	Ulceration
17	37	F	Ileum. Submucosal muscle	1 by 0.5	−	−	Acini, ducts	—	—
18	65	M	Gall-bladder. Fundus	0.7 by 0.5	−	−	Ducts with dilatation	Little	No cholecystitis
19	62	M	Gall-bladder. Fundus	1 by 1	−	−	Ducts with dilatation	Some	No cholecystitis
20	53	M	Ileum. Submucosal muscle	1 by 1	+	−	Ducts with cystic dilatation and cystic intra-ductal papillomatous proliferation	Hypertrophied; distorted	—
21	45	M	Pylorus. Submucosa	1 by 1	+	−	Acini, ducts with dilatation	Hypertrophy	—
22	62	F	Pylorus. All coats	1.5 by 1 by 8	++	+	Acini, ducts with dilatation	Hypertrophy	—
23	78	F	Gall-bladder. Fundus	Small			(No sections)	—	No cholecystitis
24	50	M	Ileum. Submucosa	1 by 1 by 0.5	−	−	Acini	Hypertrophy	Acute inflammation

served by other writers. The adenomyoma group of lesions predominates in the gall-bladder. The absence of inflammatory lesions in the wall of the gall-bladder is worthy of note. It is suggested that the single instance in which chronic cholecystitis was found represents a coincidental lesion. Table 2 offers a résumé of clinical and pathological features of the cases in this series.

The complications noted in this series were those of obstruction, ulceration, and inflammation. In case 2 a nodule strategically situated at the ampulla of Vater was accompanied by marked fibrosis, with stenosis and obstruction at the ampulla. An ascending cholangitis, with empyema of the gall-bladder, rupture, and generalized peritonitis, was the direct result of the obstructing tissue mass. In case 14 large numbers of inflammatory cells were seen in the pyloric mass. In addition to acute catarrhal inflammation of the duct structures in the nodule seen in case 24, a diffuse exudative inflammatory change was seen in the muscle. In case 16, an ulceration .5 cm. in diameter was observed at the summit of the nodule located in the submucosa of the duodenum. The latter three cases were unaccompanied by symptoms attributable to the masses.

The nodules showed histological features characteristic of normal pancreas. Zymogen granules were occasionally prominent. Direct transition of duct structures to Brunner-like glands was noted in case 6. Histopathological features commonly seen in the normally situated pancreas were encountered in the ectopic foci. Thus, chronic interstitial inflammation was seen in case 4, and inspissated eosinophilic secretion within dilated duct structures, and metaplasia of acinar to islet tissue were observed in case 12. Of interest was the observation in case 10 of focal atrophic changes in the acini with simulation of nerve structure in cross section. Epithelial hyperplasia with papillary infolding of duct epithelium was seen in case 24.

The muscular component was variable in amount and orientation. In many cases, such distortion had taken place that it could not be ascertained whether or not the muscle was an integral part of the nodule or merely residual or hypertrophic muscle of the intestinal tract. In case 6 a small zone of "xanthoma" cells was seen deep in the muscle tissue. Extensive hyaline change of muscle tissue was noted in the large pyloric mass in case 14. In this same case, neurofibromatous-like proliferation of nerve structures was seen penetrating into the gastric mucosa. In case 13, the muscle tissue was particularly abundant, leading to the erroneous diagnosis of leiomyoma in the gross. Most of the masses in the gall-bladder, in contrast, contained thin atrophic strands of muscle, and some epithelial structures were dilated with the appearance of miniature cysts.

The finding of both aberrant fully developed pancreatic tissue and ectopic gastric mucosa in a Meckel's diverticulum in case 23 parallels the case reported by Black and Packard.

The theories of formation of islands of aberrant tissue in the gastrointestinal tract have been reviewed by Branch and Gross, and by Clarke.

Most authors subscribe to the theory of inclusion of epithelial islands from the region of the embryonic foregut. Whether this explanation does apply to all the gall-bladder nodules is open to question. The finding of muscle elements has been attributed to similar inclusion of embryonal muscle cells at the time of separation of the epithelial focus. The possibility that the muscle components represent hypertrophic changes in the muscles of the wall of the involved portion of the intestine cannot be ruled out in all cases.

If it is assumed that the masses described above are of embryonic origin, and that the aberrant epithelial tissue is capable of differentiating into many different forms of glandular structures, then the term "myo-epithelial hamartoma" should be applied. In the adenomyomatous nodules, the duct structures resemble closely pancreatic and bile ducts, and may represent displacement of the latter during development. Although the distinct possibility exists that the appearance of adenomyoma may be simulated by widespread atrophy of acinar tissue in an aberrant pancreatic mass, no such complete transformation has been demonstrated. In one instance, localized atrophy of this nature was noted.

Conclusions

1. Twenty-four cases of aberrant nodular masses of ectopic differentiated epithelium and muscle in the gastrointestinal tract are described.

2. The variations in the epithelial structures and muscle tissue are indicated.

3. It is suggested that Clarke's designation of such masses as "myo-epithelial hamartomas" be adopted.

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THE CULTIVATION OF PHYSIOLOGICAL RELAXATION *

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A PERUSAL of medical journals today, as compared with a decade ago, indicates a growing recognition of the problems of relaxation. Most commonly it is linked with the discussion of hyperemotional states, noted when the patient is excitable, fatigued or hypochondriac; the need of "calmness and poise" is being stressed in a variety of disorders so wide as to include not only essential hypertension, coronary occlusion, bronchial asthma and neuropsychiatric states but also spastic colitis and even common forms of constipation.[1]

Knowledge of the problem of relaxation would seem to be spread wide, but extremely thin, in the sense that the physiological aspects of this difficult subject receive scant current attention. It is not commonly realized how well defined and also how technical the field has become. Many physicians still think of relaxation in terms of hobbies, sports or warm baths, and they believe that daily rests are the most effective measure available for the reduction of nervous irritability and fatigue states. Recent investigations fail to support this belief and have called attention once more to the diminution of neuromuscular hypertonia and residual tension as the distinguishing mark of physiological relaxation.[2] This accords with previous clinical studies, which suggested that relaxation can be cultivated in patients to replace states of excitement, emotion or neuromuscular hypertension.[3] Measurement of neuromuscular states in patients, before and after training to relax, confirmed this suggestion. Evidence has been growing that a greater reduction of nervous irritability and of fatigue states is secured if relaxation is cultivated according to physiological methods.[4]

This procedure is carried out along pedagogical lines similar to those followed in schools and colleges in teaching other skills. Methods of suggestion as practiced in psychotherapy are strictly avoided. After each period of instruction which lasts about 50 minutes, the patient customarily practices at home for like periods.

In most instances, the patient is requested to live a full, normal life, rather than to reduce his working hours. Unless it is necessary, the physician does not advise him to "go slowly," or to avoid rush and strain, since the purpose of treatment is to enable him to meet his environment rather than to escape from it. Only in cardiac and other dangerous organic conditions are the range and character of daily activities generally limited.

In acute cases of nervous disturbance, one or two treatments may be indicated to reduce the reactions. The results may then resemble those fol-

* Received for publication June 12, 1942.
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lowing the brief administration of sedatives. Inspection of the excited patient reveals when and where he is excessively tense in his skeletal musculature. The attending physician points out these regions and leads the individual to note what he is doing muscularly. He shows him where and how he is maintaining his nervous excitement by his own voluntary muscular activity. Under direction, the patient increases the tensions noted; for example, if he is frowning excessively, he increases the act till he becomes clearly aware of it. Thereupon he is instructed to discontinue what he was doing, both (1) abruptly and (2) slowly and progressively. Repeated practice is given until the over-active muscle groups have evidently become more relaxed.

In chronic conditions, the procedure follows an anatomical order, including the chief muscle groups of the limbs, trunk, neck and head. This order is often as follows: Left arm flexors, left arm extensors, left wrist flexors, left wrist extensors, right arm similarly, left foot flexors, left foot extensors, left leg flexors, left leg extensors, left thigh flexors, left thigh extensors, abdominal group, back extensor group, respiratory muscles, shoulder retractors, pectoral group, shoulder elevators, neck groups, frontalis (wrinkling), corrugator (frowning) lid and eye muscles, facial muscles, speech muscles. Those of the eyes and speech require most detailed instruction, for these participate characteristically in mental activities. Physiological evidence has supported the view that fears and anxious mental states can be relaxed away.

The patient can learn to recognize when and where he is tense if he observes carefully while he contracts the chief skeletal muscle groups one at a time during successive periods of instruction. For example, during the first period, after he has been lying quietly with eyes closed for about five minutes, he bends the left arm at the elbow, noting the sensation from muscular contraction in the flexor muscles. He is then requested to discontinue what he has been doing until no trace of this sensation remains. As a rule most of the first hour of instruction is devoted to repeated contraction and relaxation of the muscles that flex and extend the left arm. When tension has once been recognized in these localities, it becomes easier to recognize the same sensation elsewhere as a guide to relaxation.

Drill is required before the patient learns to distinguish between sensations of muscular contraction ("tenseness") and other classes of sensations, particularly those from tendons and joints. He observes that whenever and wherever he contracts, it is he who is doing it: there is always effort; but if he discontinues that doing, it is the negative of effort. The novice, however, wrongly tries to relax with effort, but in so doing, he contracts muscles, thereby frustrating his aim. In the same way the insomniac and the nervous person, incessantly seeking comfort through a series of efforts, perpetuate their own overactive states.

In medical practice, the patient may be nervously reëducated in the manner sketched above over a period of months or longer. The sedative habit

is broken. It may require 18 months to train a fatigued or nervous patient to the point where electrical records indicate an habitual state of relaxation in most skeletal muscles. However, it is customary to devote the second half of this training to the sitting position, in order to condition him so that he may become less tense and less excitable during his daily pursuits.

The scientific understanding of procedures employed in disease requires that they be tested also under normal physiological conditions, if possible. Accordingly, we here inquire whether neuromuscular relaxation can be cultivated in states of health.

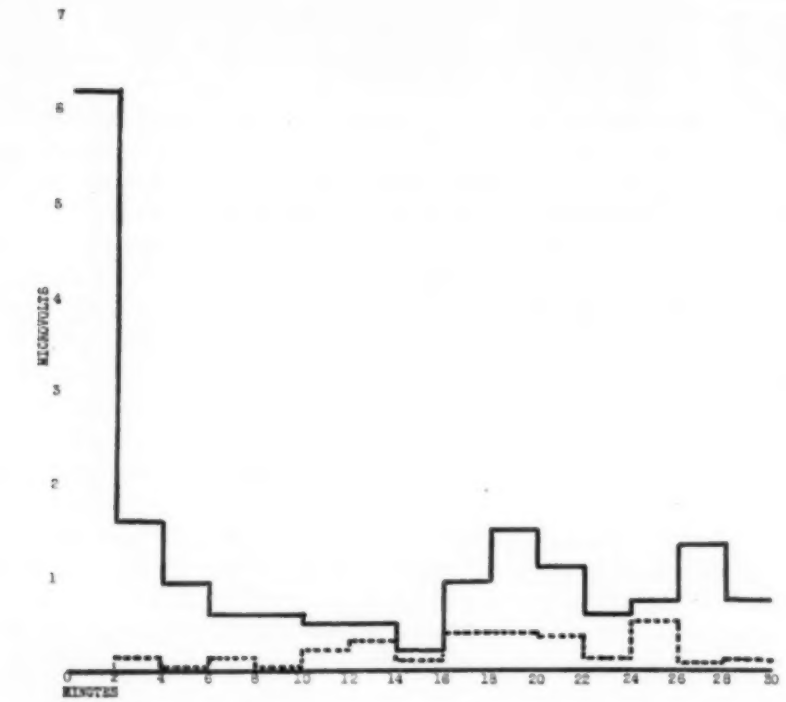
For this investigation, seven individuals were available, women instructors in physical education (Y. W. C. A.) excepting one, who was a physiotherapist. Their ages varied from about 22 to 40 years. Four of the seven were single. All appeared to be in normal spirits, able to "relax" in the sense employed in the gymnasium, but none had received technical training in physiological relaxation. Accordingly, they registered for a course of instruction, affording opportunity for the present study, the purpose of which they did not know.

All tests were performed in a quiet room in the sitting posture, while the subject read a current periodical in good light. No exchange of words occurred once the test was begun. The left foot was supported on a rest, whereas the right hung freely. Finely pointed platinum iridium wires, 0.011 inch in diameter, were employed as electrodes. After being sterilized with alcohol, they were inserted perpendicularly in the midline of the upper surface of the right thigh to a depth of approximately 11 millimeters, usually about two inches apart. The lower electrode generally was about two inches above the patella. No noteworthy discomfort results from the presence of these very fine wires. As a rule, they can be withdrawn without bleeding. Contractions in the vastus femoris, particularly the medial portion, were recorded quantitatively in electrical terms. This can now be accomplished without recourse to photography, conveniently for medical purposes, by use of the Integrating Myovoltmeter.[5] The action-potentials are amplified (within a frequency range of 20–4000), rectified and averaged in voltage at intervals of time. Two minute intervals are employed in the present investigation.

The first recording was made before the subjects received any technical instruction in relaxation, the second 10 to 12 weeks later, following seven periods of training in the lying posture. (There had been also three lectures.) This was their first experience at recording. Instruction by methods described previously was limited to the chief muscle groups of the limbs. The subjects generally reported that they practiced 30 to 50 minutes daily, but with omissions.

In figure 1 is shown the graph for an individual (E) showing microvoltages higher than most of the others before training. The curve (unbroken line) begins with a microvoltage averaging above 6 during the first two minutes of recording while reading, but descends to about 1.5 during

the second two minutes, following an irregular course mostly from 0.5 to 1.5 during the remaining 26 minutes. After training, it is evident that the muscle tested is on the whole very much more relaxed during the 30 minute period, for the tracing (broken line) runs throughout 28 minutes below 0.5 microvolt.



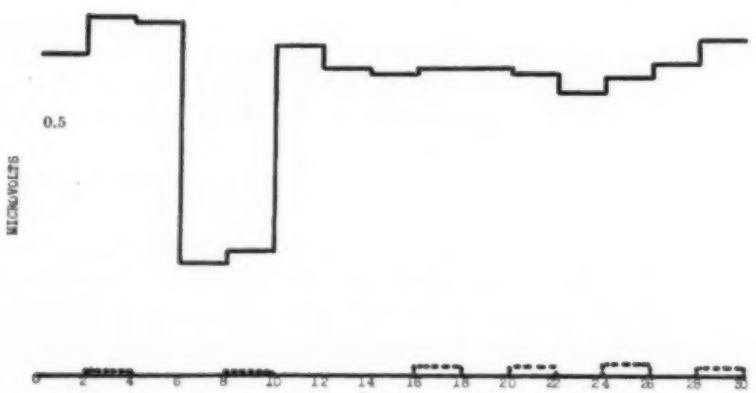


FIG. 1. (*Above*) Graphs for Subject E before training (unbroken line) and after (broken line).
FIG. 2. (*Below*) Graphs for Subject D before training (unbroken line) and after (broken line).

In figure 2 appears the graph for the individual (D) showing the lowest microvoltages before training. It runs fairly horizontally between 0.6 and 0.8 microvolt, excepting from min. 6–10, during which it is between 0.2 and 0.3 microvolt. Low as are these initial values, there is nevertheless a striking fall in the curve after training; for then the values are approximately

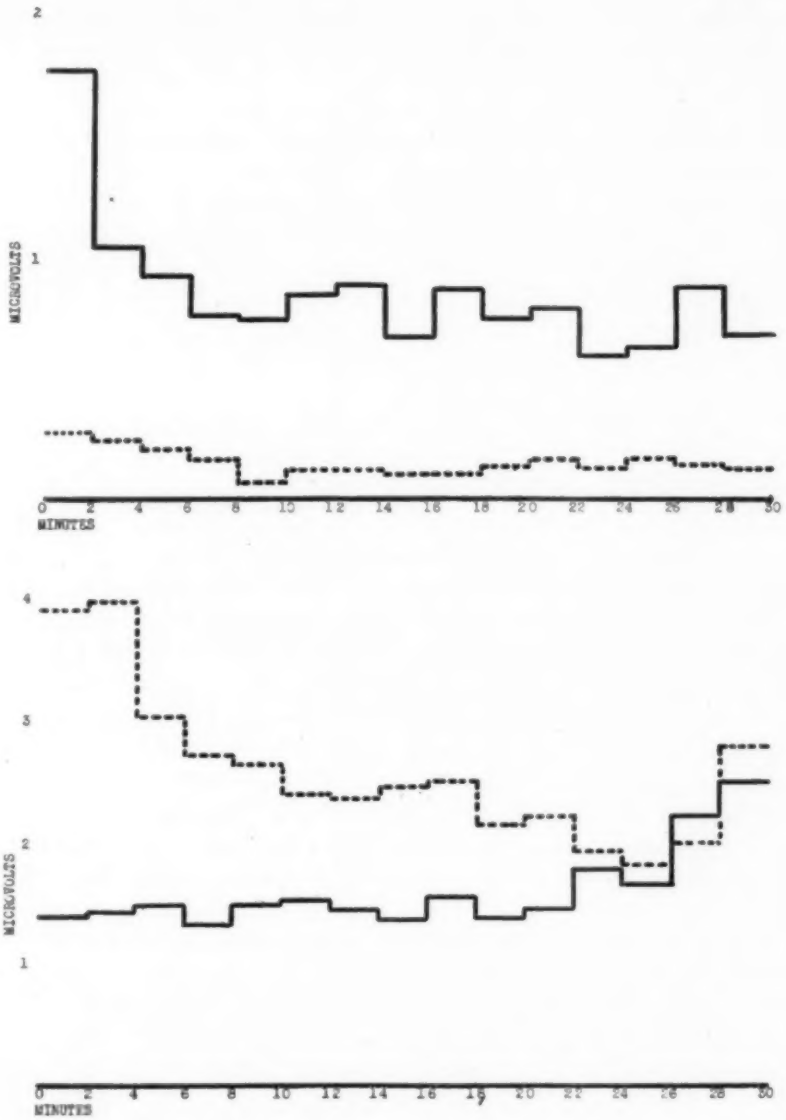


FIG. 3. (*Above*) Composite graphs for seven subjects before training (unbroken line) and after (broken line).

FIG. 4. (*Below*) Composite graphs for 10 subjects employed as controls before (unbroken line) and after (broken line) an interval of time approximately equal to that of the training course.

zero. The differences between them and zero are negligible, for they lie within the errors of the instrument. Declines similar to those shown for subjects E and D appear in the curves for the other subjects after training.

Before training, the composite curve for all the subjects, shown in figure 3, extends at 0–2 min. approximately at 1.8 microvolts; thereafter it lies mostly between 0.3 and 1.05 microvolts, nowhere falling below 0.3. After training it shows fewer irregularities, extending throughout its course below 0.25 microvolt.

TABLE I

Averaged Contraction Microvoltage for the 30 Minute Period of Test

Subject	Tests		Subject	Control Tests	
	Before Training	After Training		First Record	Second Record
A	.63	.08	1	3.01	1.17
B	.66	.30	2	1.83	.25
C	.68	.08	3	1.23	.47
D	.61	.08	4	1.48	.53
E	1.20	.18	5	.98	1.44
F	1.21	.30	6	1.93	3.75
G	.85	.08	7	.25	5.62
Aver. of All	.83	.15	8	2.04	5.92
			9	1.34	6.26
			10	1.78	.35
			Aver. of All	1.58	2.57

Table 1 shows (first three columns) the microvoltages averaged for the entire 30 minute period, before and after training. As judged by these averaged electrical measurements of tonus or contraction in the right quadriceps femoris muscles, as well as by the curves, the individual was more relaxed after training than before training.

The foregoing evidence, however, is not complete proof that the increase in relaxation was the result of training. It is necessary to run control tests under similar conditions with other normal individuals and a similar interval of time between two recordings, but with no training. This has been done in ten instances, six women and four men, ranging in age from 23 to 61 years.

In only four out of these 10 instances do reductions in contraction voltages occur on the second reading, affording graphs entirely similar in appearance to those of the preceding figures. Perhaps these individuals became adapted to the conditions of test, showing a certain increased relaxation while reading. However, in four other subjects precisely the opposite relationship holds; the second set of readings runs considerably above the first. In the two remaining individuals of this control group, the broken and unbroken lines cross each other. In one of them the second recording on the whole is the more irregular and reaches levels over five times the higher; in the other, the second recording is much higher for the first four minutes, but much

lower for the rest of the period. Figure 4 contains the composite control records for the first and second recordings. On the whole the second recording proves distinctly higher than the first, the reverse of what occurred in the test subjects after training (figure 3).

In the last three columns of table 1 are presented the averaged microvoltages for the control group. These averages show no reduction in contraction potentials in the control group upon the second recording. If the control group shows negative results, both in the averages and in the curves considered, it seems safe to conclude that the increased relaxation found in the test subjects was due to the training course.

During the present investigation, the subjects were always measured while reading in an unsupported, upright position, not lying on their backs with eyes closed as they were during the training period. Under these conditions, since the muscular region measured showed greater relaxation after training, the effects of training evidently were carried over from the lying posture, in which training was given, to the sitting posture in which the tests were made. The carry-over or "conditioning" which has been frequently noted in clinical practice of relaxation for therapeutic or preventive purposes can to this extent be confirmed.

Another matter can be noted. During reading, each individual necessarily contracted various muscles from time to time, including the arm muscles to hold the periodical, the back muscles to sit up, the neck muscles to keep the head erect, the eye muscles to see the words and to follow the lines and doubtless certain other muscles as well. However, the vastus femoris muscles evidently do not fall into the category of muscles indispensable to the act of reading in the sitting posture. They can be relaxed while such an act goes on. Relaxation during activity is known in the physiological literature as "differential relaxation." The present results are reminiscent of certain tests made on university students while reading.[6] No training in relaxation was given, but the students for the most part became more relaxed, as measured by a decline in the knee-jerk, as the hour of test wore on. This apparently illustrated a process of adaptation.[7] Such adaptation, we find, may arise automatically, as in the students mentioned, or may be pedagogically cultivated, as in the present group of subjects.

Summary and Conclusions

1. Action-potentials were measured in seven "normal" subjects before and after seven hour periods of technical training in physiological relaxation. The interval between the two sets of measurements was about 10 to 12 weeks. Electrodes were inserted in the right quadriceps femoris muscle region, while the right foot hung freely. Throughout each period, the subject read a periodical.

2. The action-potential curves and the average values were markedly reduced following the training.

3. No such reductions were found in most of the control tests under similar conditions with other subjects who received no training.

4. It is confirmed again that the results of technical training in relaxation are quantitatively demonstrable.

5. All measurements were made in the sitting posture, while reading. Evidently, training procedures administered in the lying posture can recondition the neuromuscular state in other postures. Training in general relaxation can contribute toward differential relaxation.

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PERFORATION OF THE INTERVENTRICULAR SEPTUM FOLLOWING INFARCTION; INTRAVITAM DIAGNOSIS

REPORT OF A CASE AND SURVEY OF THE LITERATURE*

By MANUEL L. WEBER, M.D., *San Francisco, California*

DESPITE the ease with which a correct diagnosis of rupture of the interventricular septum, occurring in the course of cardiac infarction following coronary thrombosis, could be made during life, if the characteristic criteria of the diagnosis of this complication are borne in mind, only in very rare instances has the condition been recognized clinically, as indicated by the meager reports in the literature. For almost a century, from 1845, when Latham [1] first described rupture of the infarcted septum of the heart, to Sager's [2] comprehensive survey of the subject in 1934, only 18 instances of this type of septal perforation were recorded in the literature, despite the seemingly increasing incidence of coronary thrombosis throughout the world. Through a careful search of the literature, both domestic and foreign, to 1942, I was able to collect 16 additional cases, bringing the total number on record to 33, which testifies to the rarity of the condition. Surprisingly small as the number of such cases found at the autopsy table seems to be, the number correctly diagnosed during life and subsequently confirmed by necropsy is much smaller, there being only five. The purpose of this report is to review the subject completely up to date and to present another case of perforation of an infarcted septum recognized antemortem.

CASE REPORT

U. U., a World War I veteran, aged 46, had always been in good health except for frequent "colds" during the preceding two or three years. He was active as an automobile salesman and had led a normal social life. About three months prior to the onset of his last illness, during one of his "colds," he was examined by a physician and was told that his blood pressure was somewhat high and that his pulse was rapid. He returned for reëxamination two weeks after the "cold" cleared up and was assured that there was nothing wrong with his heart, whereupon he returned to work. On September 24, 1941, he was awakened during the early hours of the morning with moderately severe substernal pain, which lasted about one hour and a half, and which was accompanied by a sense of oppression and dyspnea. However, the pain gradually subsided and, although the patient felt somewhat tired in the morning, he went to work as usual and continued at it for three days. On the third day, shortly after supper, he was suddenly seized with severe, "excruciating" pain in the midsternal and epigastric regions with a projected ache in both arms. "I felt like some-

* Received for publication March 30, 1942.
From the Medical Service, Veterans' Administration, San Francisco.
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one was pulling a bundle of nerves." The pain persisted all night, fluctuating in severity. There was no nausea or vomiting but the patient perspired freely and became rather apprehensive and dyspneic.

He first attended the outpatient clinic on September 29, where he was examined and an electrocardiogram and a roentgenogram of the chest (figure 1) were taken. The record of the outpatient examination failed to mention any pathological cardiac signs. The heart was not enlarged. The blood pressure was 150 mm. Hg systolic and 100 mm. diastolic. The rhythm was regular. The rate was 92. No murmurs were recorded. A roentgenogram of the chest revealed a small area of calcification near the base of the right lung; otherwise it was normal. The patient did not desire to

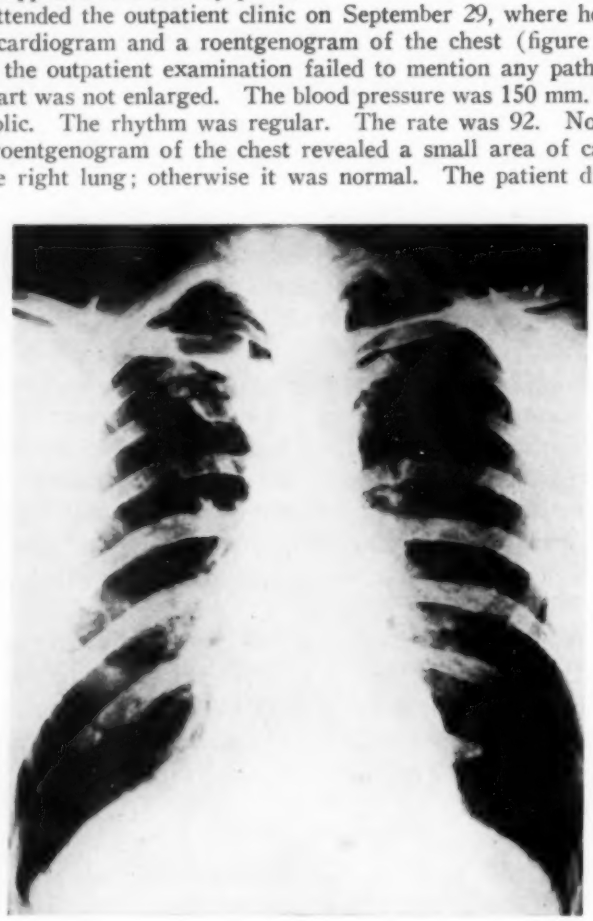

FIG. 1. Roentgenogram of chest taken September 29, 1941, showing normal cardiac shadow.

enter the hospital then, but returned to his home in Sacramento (100 miles by auto). While there he continued having thoracic pain and dyspnea. He was finally admitted to the hospital on October 3, 1941, nine days after he suffered the first attack.

Physical Examination. When examined by me on October 3, the patient was sitting in a semirecumbent position. He was slightly cyanotic, very apprehensive and restless, pointing toward the chest to indicate pain. He was moderately dyspneic. There was slight distention of the external jugular veins. The liver edge was palpated 4 cm. below the costal margin and was tender to pressure. There was no peripheral edema.

The heart did not appear to be enlarged to percussion. There was a very loud, rough systolic murmur audible over the entire precordial area, maximal to the left of the sternum in the fourth and fifth interspaces. The murmur was also audible at the left subscapular region. There was a palpable systolic thrill over the ensiform area

and in the same locality where the murmur was maximal. There was no diastolic murmur at any point. The pulmonic second sound was louder than the second aortic. The rhythm was regular. The cardiac rate was 118, and the blood pressure was 110 mm. Hg systolic and 90 mm. diastolic. When he was first seen, no râles were made out in the chest but within a few days the patient developed numerous crackling râles in the right chest from the sixth rib down. Diminished breath sounds appeared over the bases.

Laboratory Findings. Several urinalyses were done, all of which revealed variable amounts of albumin ranging between one plus and a trace. There were a few hyaline casts. The total leukocyte count of the blood was 13,900 with 67 per cent polymorphonuclears. The erythrocyte sedimentation index was 28 mm. per hour by

FIG. 2. Roentgenogram taken October 11, 1941, showing cardiac enlargement and passive congestion through the lungs.

the Cutler method. On October 5 the temperature rose to 101° F., but from then on it was somewhat subnormal. The arm-to-tongue circulation time performed with decholin was 30 seconds. The venous pressure by the direct method was elevated to 16 cm. of water. Two days before his death the urea nitrogen was 68.1 and creatinine 2.7 mg. per 100 c.c. of blood. The Wassermann reaction was negative. The electrocardiogram (figure 3) was repeated on October 13 and showed a deviation in the main electrical axis to the right and changes in the T-waves in all leads, characteristic of the evolutionary pattern of an acute cardiac infarction. Bedside roentgenogram of the chest (figure 2) was repeated on October 11. Allowing for a certain amount of distortion due to the position in which the roentgenogram was taken, it was nevertheless apparent that compared with the previous film the heart was enlarged in size and the hilus shadows had become more prominent, both in density and size, apparently because of passive congestion.

Course of the Disease. Throughout his stay in the hospital the patient's course was progressively downward. He was constantly dyspneic and orthopneic. When placed in an oxygen tent he became "panicky" and asked to be removed. On October 9 he began to complain of "pins and needles" in the sole of the left foot and in the toes. He could not tolerate the weight of the covers. Both lower extremities were cold and gray-cyanotic, the left more so than the right and up to a higher level. "Beer spots" appeared on both feet. The pulse of the main arterial vessels of the feet

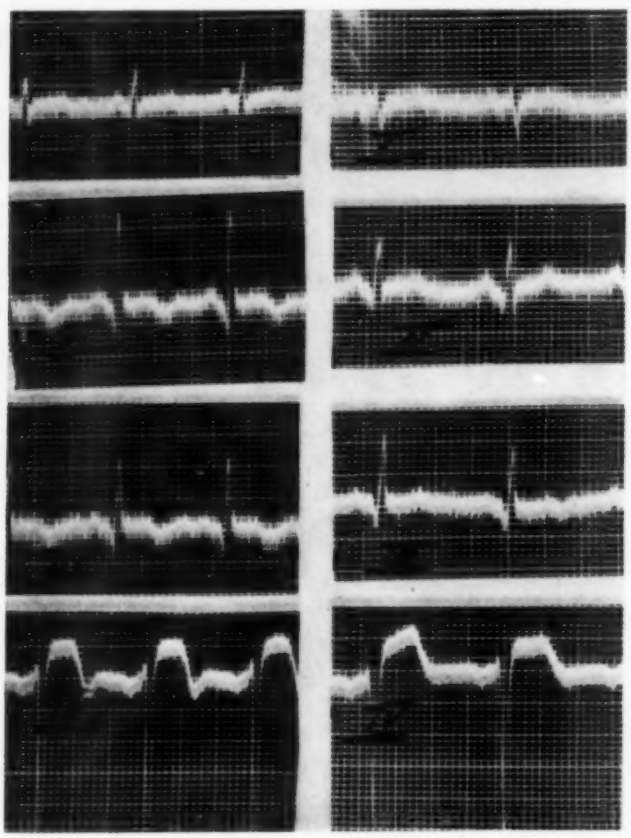

FIG. 3. Initial and final electrocardiograms. (a) 9/29/31—Leads II and III show presence of prominent Q-waves, negative T_2 and T_3. IVF shows small R, elevated S–T, and negative T. Normal axis deviation. (b) 10/13/41—Diphasic T_1, prominent Q_3. IVF—Large Q, elevated S–T and negative T. Right axis deviation.

was absent but the popliteal arteries pulsated strongly. Two days later both hands became deeply cyanotic and cold, although there was a good pulse in the radials. Early dry gangrene of all the toes of the left foot made its appearance toward the end. He developed slight pitting edema of both feet. Dullness and râles at the bases of both lungs became more marked. While at first the patient was irritable and restless, toward the end he became indifferent, only complaining of pain in the chest and feet when directly questioned. The cardiac signs, including the murmur and thrill, persisted unchanged until death. The patient died in shock on October 15, 1941, twenty days after the initial attack.

Antemortem Diagnosis. The diagnosis of cardiac infarction following coronary thrombosis was practically certain from the day of the patient's admission to the hospital on the basis of the history and electrocardiographic findings. An additional diagnosis of rupture of the interventricular septum was entered for reasons to be discussed later. In the course of the illness there appeared evidence of right heart

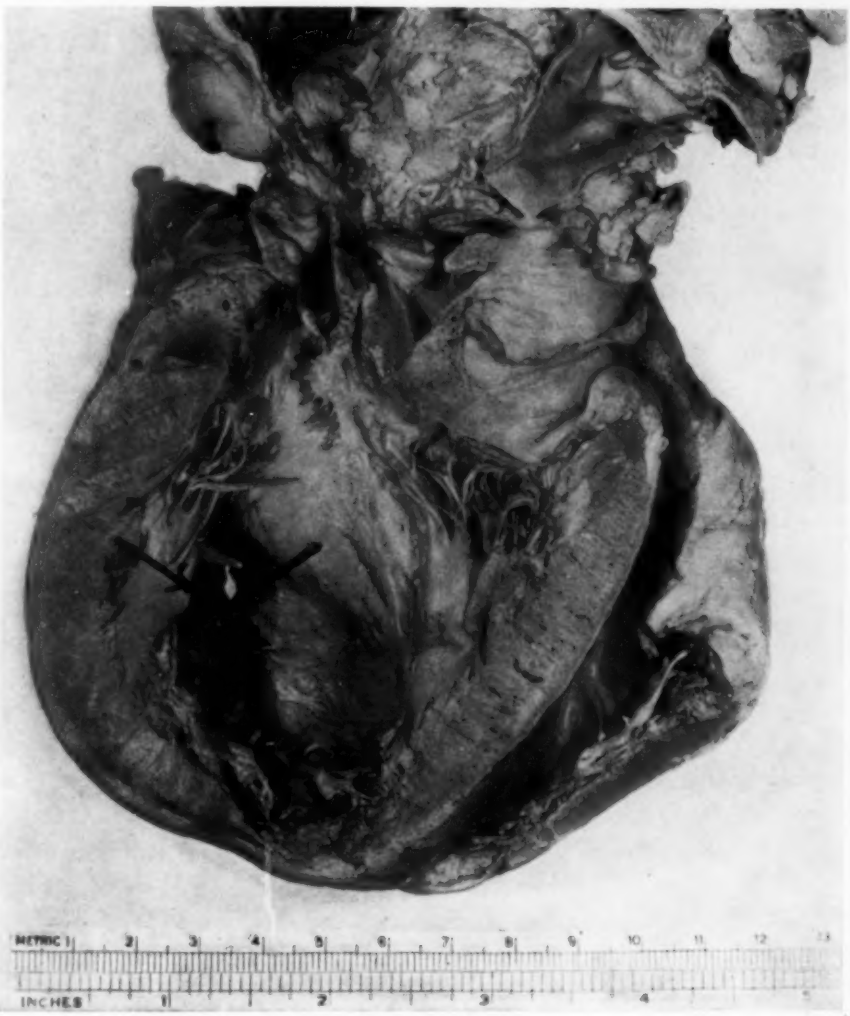

FIG. 4. Anterior view of the heart looking into the left ventricle, showing aneurysm of septum and perforation.

failure in addition to left heart failure with which the patient came to the hospital. The peripheral vascular symptoms might be regarded as resulting from multiple emboli, were it not for the unusual involvement of all four extremities in the absence of embolism to other organs such as the brain, kidneys or spleen. Fishberg [8] pointed out that shock may, in rare instances, cause peripheral circulatory failure of such a degree as to result in peripheral symmetrical gangrene. Unfortunately, the source of the beginning gangrene in this case was not found at postmortem examination, but

from its symmetry—all four extremities—one can surmise that it was not due to embolization, but rather to peripheral circulatory failure caused by weak heart action.

Clinical Diagnosis. (1) Massive cardiac infarction with perforation of the interventricular septum. (2) Peripheral circulatory failure.

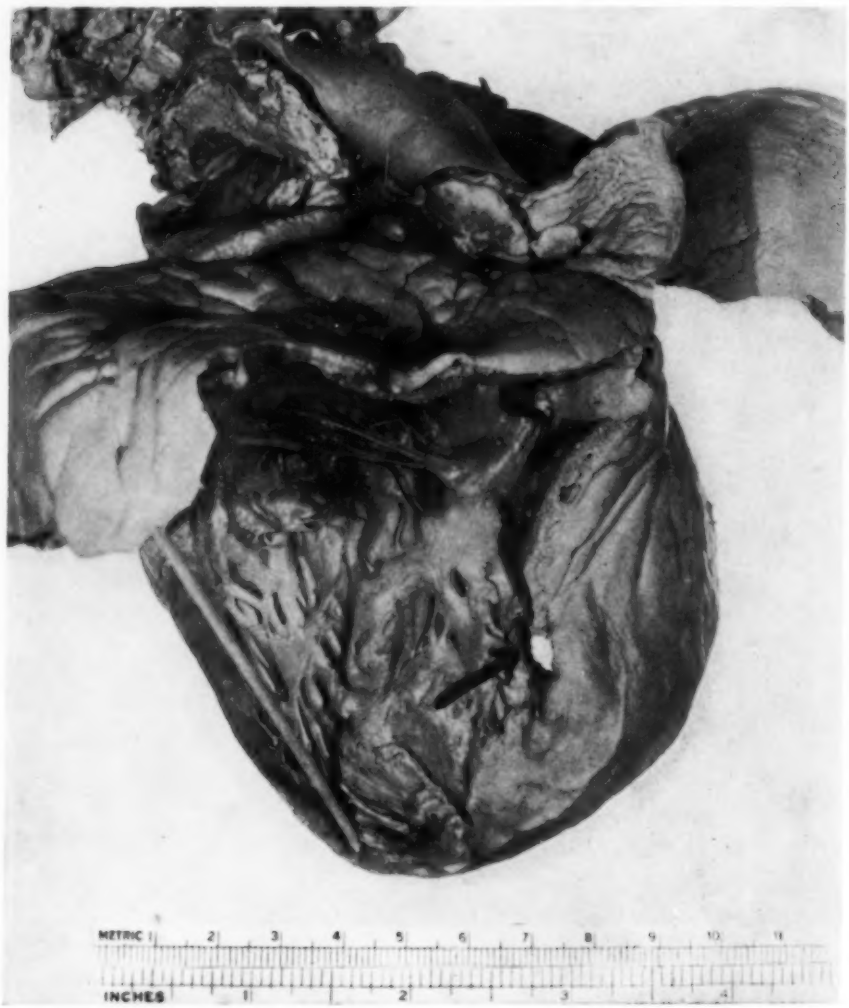

FIG. 5. View of the heart looking into the right ventricle, showing perforation, communicating with left ventricle.

Postmortem Examination. The fixed heart was examined by Dr. Eichorn, University of California Hospital, who reported as follows:

Gross Description. The specimen was a fixed heart and part of the aorta cut open to expose the chambers. The organ weighed 454 grams. There was infarction of the lower half of the interventricular septum and the immediately adjacent anterior apical portions of the ventricles. The infarcted half of the septum bulged into the right ventricular chamber producing an aneurysmal dilatation in the lower part of the

left chamber about 4 cm. in diameter. In the anterior portion of this dilatation there was a rupture of the septum 1 by 2 by 2.3 cm. in size at a point 5.5 cm. from the apex. This established communication between the right and left chambers. No massive mural thrombi were present, although there was thrombotic material attached to the trabeculae carneae at the apex. The epicardium was smooth.

The left ventricle measured 1.8 cm. in its thickest part and 0.5 cm. at the apex. The right ventricle measured 0.7 cm. in its thickest part and 0.15 cm. close to the septal rupture. The coronary arteries showed atherosclerotic thickening.

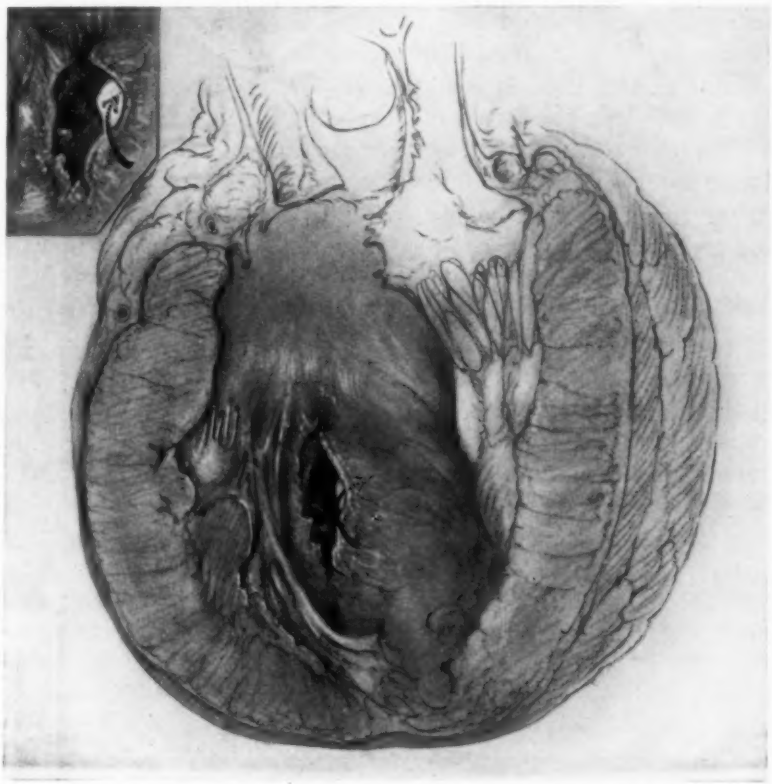

FIG. 6. Schematic drawing of the heart looking into the left ventricle; in the left upper corner a miniature drawing showing the opening from the right ventricle.

The valves grossly were not remarkable and except for the small thrombotic masses at the apex the endocardium was smooth.

Microscopic Description. The myocardium was hypertrophied and in the apical sections of the ventricles and septum the muscle was infarcted. Here the endocardium bore a mass of thrombus which showed early organization. The epicardial surface bore considerable fat which was increased in cellularity. There was no exudation on the epicardial surface. Scattered groups of small round cells occurred immediately beneath the epicardium in all of the sections. The coronary arteries showed considerable atheromatous thickening which was most marked in the anterior descending branch. This vessel had a crescentic lumen with dilation approximately ⅓ the combined thicknesses of the walls. There was much lipoid accumulation and fatty acid deposition beneath the thickened intima.

Anatomical Diagnosis. I. Arteriosclerotic heart disease with: A. Infarction of the epicardial portions of the right and left ventricles and interventricular septum. B. Aneurysmal dilatation and rupture of the interventricular septum anteriorly into the right ventricle at the apex.

Review of the Literature from 1924 to This Date

Kepler, Berkman and Barnes [4] reported a case of a man, aged 60, who was taken ill with severe substernal pain projected to the wrists. There was a marked systolic murmur over the entire precordium with its point of maximal intensity in the fourth and fifth interspaces and a sharp thrill to the left of the sternum. He went into a state simulating shock, characterized by a rapid fall in blood pressure, cyanosis and dyspnea. At necropsy there was an acute infarction of the apex, anterior portion of the left ventricle and of the adjacent interventricular septum, the infarction extending two-thirds of the distance from the apex to the base. In the lower part of the septum there was an irregular rent about 1 by ½ cm.

The patient of Master and Jaffe [5] was a woman of 65, who had had hypertension for at least four years. She was awakened from sleep experiencing a sensation of nausea. A few days later she collapsed while trying to get out of bed. She was dyspneic, cyanotic and perspired profusely. Her blood pressure dropped. There was a loud systolic murmur at the apex. There was no evidence of congestive failure. The electrocardiogram was characteristic of a coronary occlusion involving the posterior wall of the left ventricle. She died 11 days after being taken ill. Postmortem examination: Acute thrombosis of the posterior descending branch of the right coronary artery with myomalacia and pinpoint perforation of the posterior portion of the interventricular septum at the apex. The left anterior descending and circumflex arteries were narrowed. General arteriosclerosis was marked.

The case observed by R. Nadler [6] was a woman of 42, an inmate of an institution for the insane, who complained of dizziness, vomiting, cramp-like pain in the stomach and gall-bladder region. The heart was enlarged. There was a loud systolic murmur over the entire precordium. The blood pressure was 145 mm. Hg systolic and 110 mm. diastolic. She died the following day. Postmortem examination revealed a diffuse softening of the anterior wall of the left ventricle. Five centimeters above the apex there was a perforation of the septum. There was generalized coronary sclerosis and small thrombi in the left circumflex coronary artery.

Mahrburg's [7] patient was a man of 55 in apparent good health who had a sudden attack of severe chest pain radiating into the arms. He became weak and dyspneic. The heart was enlarged. There was a systolic murmur over the entire heart, best heard over the apex, and a systolic thrill. The blood pressure was 85 mm. Hg systolic and 8 mm. diastolic. The liver was enlarged and painful to pressure. One month later he developed a complete heart block and died. At necropsy the heart weighed 400 gm. The orifices

of the coronaries were free. There was marked thickening of the arterial wall of the left descending coronary and narrowing of its lumen for a distance of 2.5 cm. Four centimeters above the apex there was a defect in the septum in the form of a deep indentation, on the bottom of which there were four small openings communicating between the left and right ventricles. This case is distinct from the others in the reviewed series in that the septal defect caused the development of a complete block by interrupting the auriculoventricular pathway of impulses.

The two cases described by Bickel and Mozer [8] differ in several respects, the first being "silent" and the other having marked symptoms.

Case 1. A man of 87 enjoyed perfect health until 15 days prior to admission when he began to complain of weakness and loss of appetite. He developed a cough and became dyspneic. At no time did he have the least thoracic pain. There was no cyanosis and no edema. His respiration was of the Cheyne-Stokes' type. The heart was normal in size to percussion. The apical thrust was imperceptible. The sounds were feeble. There were no murmurs and no thrills. The blood pressure was 150 mm. Hg systolic and 70 mm. diastolic. There were signs of bronchopneumonia. The patient was disoriented and restless. During the five days in the hospital no new symptoms were apparent. Weakness rapidly increased. His blood pressure dropped gradually and he died in semicoma. Postmortem examination revealed an enlarged heart. The apex of the left ventricle was thinned out to 5 mm. forming an aneurysm. There was an oval opening 2 by ½ cm. in the septum at the level of its attachment to the posterior wall of the myocardium, permitting a large communication between the two ventricular cavities. The left coronary artery was completely obstructed by a thrombus at the level of its descending branch, 2 cm. from its origin. Another thrombus incompletely organized occupied the right coronary artery at the level where it curves to enter into the posterior ventricular groove.

Case 2. A man, aged 60, was admitted to the hospital in a state of weakness and intense dyspnea. Three weeks previously, he had developed extremely violent retrosternal pain radiating into both arms. The pain subsided somewhat but the dyspnea progressed throughout the subsequent days. His extremities were cold and cyanotic. The heart was slightly enlarged. There was a harsh systolic murmur over the entire precordium and an intense systolic thrill below the apex. The heart sounds were feeble. The blood pressure was 70 mm. Hg systolic and 50 mm. diastolic. There were râles of all sizes over both lungs. The liver was enlarged and painful to palpation. He died the day after admission. Postmortem examination disclosed a markedly enlarged heart. The valves were normal and soft, except the aortic valve which was moderately sclerosed. The left ventricle was thinned out to 3 mm. near the level of the apex. The interventricular septum was greatly thinned out in the lower ⅓ and was necrosed in the center. There was an oval opening communicating between both ventricular cavities. The left anterior and the right circumflex coronary arteries contained several atheromatous plaques. The descending branch of the left coronary was obstructed 5 cm. below its origin by thrombosis.

Huber [9] in the same year presented two cases of rupture of an infarcted septum.

Case 1. A 70 year old woman was brought into the hospital in a moribund state. She appeared to have heart trouble but no findings are given. Postmortem examination revealed a "rent" 3 cm. long in the interventricular septum, 4.5 cm. above the apex. There was thrombotic closure of the descending branch of the left coronary artery and marked narrowing of the lumen of the right coronary artery.

TABLE I

Cases of Perforated Interventricular Septum Reported from 1924 to Date

No.	Year in Which Reported	Author	Sex of Patient	Age	Presence of Murmur and Thrill	EKG Findings	Site of Perforations	Size, Forms and Number of Perforations	State of Coronary Arteries	Period of Survival Following Perforations	Recognized Ante-Mortem
1–18	1934	Reviewed by Sager	—	—	—	—	—	—	—	—	—
19	1935	Kepler et al.	M	60	Murmur and thrill	?	Lower part	1 × 1½ cm.	?	?	No
20	1935	Master and Jaffe	F	65	Murmur	Post. infarction	Post. part near apex	Pinpoint	Thrombosis of rt. cor. art. Narrowing of lt. descending and circumflex	11 days	Yes
21	1935	R. Nadler	F	42	Murmur	?	5 cm. above apex	?	Thrombosis of lt. circumflex	2 days	No
22	1935	Mahrburg	M	55	Murmur and thrill	Complete block	4 cm. above apex	4 small openings	Narrowing of lt. descending	30 days	No
23	1935	Bickel and Mozer	M	87	None	?	Level of attachment of septum to the post. wall of myocardium	2 × ½ cm.	Complete thrombosis of lt. cor.; incomplete thrombosis of rt. coronary	20 days	No
24	1935	Bickel and Mozer	M	60	Murmur and thrill	?	Lower third	?	Thrombosis of lt. descending. Atheromatous plaques in lt. anterior and rt. circumflex	2 days	No
25	1935	Huber	F	70	No findings given	—	4.5 cm. above apex	Rent 3 cm. long	Thrombosis lt. descending; marked narrowing of rt. cor.	1 day	No
26	1935	Huber	M	66	Systolic and diastolic murmur over all valves	—	Inner portion	2.5 × 1.6 cm.	Near thrombosis of lt. descending	21 days	No

TABLE I—(*Continued*)

No.	Year in									Period of	Recog-

TABLE I—(*Continued*)

No.	Year in Which Reported	Author	Sex of Patient	Age	Presence of Murmur and Thrill	EKG Findings	Site of Perforations	Size, Forms and Number of Perforations	State of Coronary Arteries	Period of Survival Following Perforations	Recognized Ante-Mortem
27	1936	Gross and Schwartz	M	57	Murmur and thrill	R.A.D.	Central portion	Several cm.	Lt. circumflex completely occluded; atheroma of rt. cor.	5½ mo.	No
28	1936	Stern	M	59	Murmur	R.B.B.B.	5 cm. from the apex	Admitting middle finger	Occlusion of descending branch rt. cor.	1 day	No
29	1937	Stanley	F	61	Murmur and thrill	Cardiac infarction	5 cm. from the apex	2 openings 12 mm. and 3 mm.	Rt. coronary almost completely occluded 2 cm. from orifice. Lt. cor. contained calcified plaques	8 months	Yes
30	1937	Kogan	F	52	Murmur	Anterior cardiac infarction	Lower part	Oblong slit	Lt. descending occluded. Rt. cor. contained small plaques	?	No
31	1937	Kogan	M	67	Murmur	Posterior cardiac infarction	Central part	2 cm.	Lt. circumflex cor. greatly narrowed. Other coronaries narrowed	?	No
32	1939	Scott and Garvin	M	56	Murmur and thrill	?	6 cm. from the apex	Funnel shaped hole	Rt. posterior descending occluded. Arteriosclerosis of other coronaries	20 days	No
33	1941	Bayley and Fader	M	47	Murmur and thrill	Cardiac infarction R.A.D.	Basal region	3 openings	Marked narrowing of first part of rt. coronary. Moderate narrowing of lt. cor.	8 weeks	Yes
34	1942	Moolten	M	57	Murmur and thrill	Acute cardiac infarction	Central part	2 openings	Lt. descending markedly narrowed. Rt. narrowed by small plaque	12 weeks	No
35	1942	Weber	M	46	Murmur and thrill	Cardiac infarction R.A.D.	Lower half	1 × 2 × 2.3 cm.	Atheromatous thickening, most marked anterior descending	2 weeks	Yes

Case 2. A man, aged 66, was an invalid for three years because of arteriosclerosis, dizzy spells and dyspnea. On January 31, 1935, he suffered pain in the heart region with radiation down the left arm. He had daily attacks from that time on. The heart was found to be enlarged. There were audible systolic and diastolic murmurs over all valves, maximal over the mitral area. The blood pressure was 80 mm. Hg systolic and 60 mm. diastolic. He died three weeks following the first attack of thoracic pain. Postmortem examination showed normal valves. At the apex there was great thinning of the left ventricular wall with an aneurysmal bulging. The inner portion of the interventricular septum contained a defect 2.2 by 1.6 cm. which communicated between the left and right ventricles. The descending branch of the left coronary artery was nearly closed by an organized thrombus.

Gross and Schwartz,[10] in 1936, described a case of a man of 57 who was suffering from hypertensive heart disease with congestive failure. The first symptoms became evident in September 1929, when he suddenly became unconscious for one and one-half hours. He was cyanotic. His breathing was stertorous and blood trickled from the mouth. During the following three months he had five such episodes. He was admitted to the Montefiore Hospital in a state of severe congestive failure with enlargement of the heart, engorgement of the cervical veins, swollen liver, bilateral hydrothorax and slight dependent edema. His blood pressure was 184 mm. Hg systolic and 128 mm. diastolic. The electrocardiogram revealed right axis deviation and slurring of the QRS complexes. There was a prolonged systolic murmur audible over the entire precordium and base of the heart and a systolic thrill over the same area. He succumbed to lobar pneumonia two months after admission. On postmortem examination the apex was found to be thinned and there was considerable fibrous tissue replacing the myocardium. The entire lower half of the septal wall was replaced by fibrous tissue and in the central portion of the septum there was a circular defect measuring several centimeters in diameter. The right coronary arteries showed considerable atherosclerosis with calcification. The anterior descending artery had two branches, both revealing marked atherosclerosis with calcification. The lumina were narrowed by large yellowish-gray plaques. The left circumflex artery was completely occluded by a firm thrombus about 1 cm. from its origin.

Stern[11] attended a man of 59 who complained of dyspnea and substernal pain for three weeks. Three days prior to admission to the hospital he suffered sharp, cutting substernal pain, radiating to the epigastrium and associated with severe dyspnea. The heart was enlarged. The sounds were faint and there was a slight systolic murmur at the apex. The blood pressure was 120 mm. Hg systolic and 85 mm. diastolic. An electrocardiogram showed right bundle branch block. Six days later his dyspnea increased, and his breathing became of the Cheyne-Stokes' type. The heart sounds were irregular. A loud systolic murmur appeared at the apex. He died the same day. At necropsy the heart was greatly enlarged. There was an area of infarction on the lateral and posterior surfaces, measuring 9 by 7 cm. There was a rent in the septum 5 cm. from the apex of the right ventricle perforating into the left ventricle, of a size which easily admitted the middle finger. The aortic cusps were thickened and calcified. The right coronary artery was normal except for calcification in the first inch. Its descending branch, about 3 cm. below the parent vessel, was occluded by a partially organized adherent clot.

The case reported by Stanley[12] which was the third on record in which the correct diagnosis was made during life, was that of a woman, aged 61, who was awakened by upper epigastric pain radiating upward into both arms, which was followed by vomiting. The heart was not enlarged to percussion and no murmurs were heard. The blood pressure was 140 mm. Hg systolic and 86 mm. diastolic. She gradually improved but three days later, while on the bedpan, she was stricken with substernal pain and went into shock with sweating, cyanosis and dyspnea. At that time there was heard a loud harsh systolic murmur accompanied by a thrill in the

fourth interspace to the left of the sternum. The blood pressure was 100 mm. Hg systolic and 60 mm. diastolic. On the basis of the clinical picture and electrocardiogram a diagnosis of coronary thrombosis was made. The patient died eight months after the beginning of her illness in a state of increasing decompensation and with a right hemiplegia. The cardiac murmur persisted until death. At necropsy the findings of congestive failure were marked. The heart was slightly enlarged. The posterior wall of the left ventricle was thinned out to 3 or 4 mm. and bulged backward forming an aneurysm. The adjacent half of the septum was composed of firm scar tissue and through its center were two oval holes 12 and 3 mm. in diameter communicating between the two ventricular cavities. The lumen of the right coronary artery, about 2 cm. from the orifice, was almost completely obliterated by a calcified plaque. The remainder of the right coronary, as well as the left coronary arteries had a moderate number of hyaline and calcific plaques.

Kogan [13] (Russia) attended two patients with rupture of the septum as the result of cardiac infarction within the short space of nine months.

Case 1. A woman, aged 52, complained of attacks of oppression in the region of the heart, pain in the right arm and scapula. She was dyspneic and cyanotic. The heart was enlarged to percussion. The sounds were faint. Blood pressure was 180 mm. Hg systolic and 120 mm. diastolic. At times there was a systolic murmur at the apex. Eight days later she suffered an attack of severe thoracic pain. Her pulse rose to 130 and there appeared a loud systolic murmur, maximal over the lower sternum. The blood pressure dropped to 125 mm. Hg systolic and 95 mm. diastolic. There appeared evidence of right heart failure. An electrocardiogram revealed the pattern of infarction of the anterior aspect of the left ventricle. She died with symptoms of progressive heart failure, and the systolic murmur remained loud to the very end. At autopsy the heart was found to be enlarged. The wall of the left ventricle near the apex was much thinned out and presented an aneurysmal bulge. The lower anterior portion of the septum contained an oblong slit connecting the ventricular cavities. The left coronary artery in its beginning contained many atherosclerotic plaques narrowing its lumen. The descending left coronary was completely occluded by thrombus. The right coronary artery was patent although it also contained small yellow plaques.

Case 2. A man of 67 developed severe pain in the heart region radiating to the back. Four days later he complained of great weakness, frequent attacks of vomiting and abdominal distention. The heart was enlarged. The pulse was weak. The blood pressure was 88 mm. Hg systolic and 70 mm. diastolic. Phenomena of right heart failure were present. There was a loud harsh systolic murmur in the fourth and fifth intercostal spaces near the sternum to the left. An electrocardiogram showed posterior infarction. He died following progressive cardiac weakness. Postmortem examination revealed the heart to be enlarged. All cavities were dilated. The valves were normal. In the central portion of the septum there was a rent 2 cm. in diameter connecting both ventricular cavities. The posterior walls of the ventricles were soft and tore easily. The aorta contained many plaques. The lumen of both coronary arteries was narrowed. The circumflex branch of the left coronary was greatly narrowed by calcification. There were no thrombi present.

In March 1939 Scott and Garvin [14] described a rupture of an infarcted septum in a 56 year old man who was admitted to the psychopathic ward because of disorientation, delusions and hallucinations which he developed following an episode of dizziness and unconsciousness. Except that there was evidence of marked arteriosclerosis, general physical examination was essentially negative. The heart was normal and the blood pressure was 135 mm. Hg systolic and 90 mm. diastolic. About six weeks later the patient developed a high temperature, dyspnea and evidence of broncho-

pneumonia. At that time over the entire precordium there was heard a loud systolic murmur which was transmitted to the base of the heart and to the left axilla and was accompanied by a sharp thrill. The blood pressure dropped to 98 mm. Hg systolic and 60 mm. diastolic. He died 20 days after the onset of his acute illness. Postmortem examination revealed a large heart weighing 550 gm. There was an irregular, funnel-shaped hole in the anterior portion of the interventricular septum 6 cm. from the apex connecting the two cavities. The edges of the lesion consisted of necrotic muscle tissue. The coronary arteries all showed marked arteriosclerosis. The right posterior descending branch was occluded but no thrombus was present.

Bayley and Fader [15] in February 1941 reported the case of a man of 47, who had experienced a sudden burning pain behind the upper part of the sternum, radiating to the left shoulder and down the left arm. The pain subsided within two hours. A few days later he was examined by a physician and was assured that his heart was all right. His blood pressure was 160 mm. Hg systolic and 120 mm. diastolic. A second attack occurred one week later with pain in the left hypochondriac and epigastric regions associated with nausea, vomiting, weakness and dyspnea. A "leak in the heart" was diagnosed by a consultant. When admitted to the hospital two weeks later the heart was enlarged. A loud, rough murmur which lasted throughout systole and a pronounced thrill were found to the left of the sternum in the fourth and fifth interspaces. The liver was enlarged and tender. Dense mottling through both bases and in the region of the hilus of the lungs was seen in the roentgenogram which was interpreted as evidence of pulmonary edema. An electrocardiogram was characteristic of a cardiac infarction. Gradually, the phenomena of right heart failure made their appearance and the patient died eight weeks after admission. The precordial thrill and murmur remained unchanged throughout the illness. Postmortem examination revealed a moderately enlarged heart and an aneurysmal dilatation of the apex of the left ventricle. The thickness of the left ventricle at the base was 14 mm., but the aneurysmal sac was thinned out to 2 mm. In the basal region of the interventricular septum there were three openings which connected the two ventricular chambers. There was marked narrowing of the first part of the right coronary artery and moderate narrowing of the left coronary artery. No area of total occlusion was found.

Finally Moolten [16] in 1942 reported the case of a man, aged 57, who suffered an attack of severe precordial pain. Two weeks later he began to experience marked dyspnea. On physical examination, the heart was greatly enlarged, there was dependent edema, the liver was swollen, the cervical veins were engorged and there were signs of right-sided hydrothorax. The venous pressure by the direct method was 23.5 cm. of water. The electrocardiogram was characteristic of an acute myocardial infarction. A loud systolic murmur and a palpable thrill were present at the apex.

The patient lived 12 weeks. At necropsy, a double perforation of the central part of the interventricular septum was found. The descending branch of the left coronary artery was markedly narrowed by calcified atheroma. A small plaque of soft atheroma in the intima of the right coronary artery caused narrowing of the vessel. The perforation was not recognized antemortem.

Comments and Conclusions

Since the description by Rogers in 1879 of the clinical symptoms of perforation of the interventricular septum, the congenital form has been amply

studied, but very little attention has been accorded to the acquired forms. The immediate causes of spontaneous rupture of the septum, aside from the type under consideration here, are either traumatic or ulcerative. To the latter belong the rare instances of septal perforation due to an ulcerative endocarditis. The site of predilection of the perforation in the congenital form is in the upper membranous part of the septum where its thinness explains its particular vulnerability. The third variety of the acquired perforation, i.e., the one resulting from an ischemic massive necrosis following thrombosis or marked narrowing of one or more major branches of the coronary arteries, has its site of predilection in the lower muscular portion of the septum. This variety, which in the majority of cases has been discovered at necropsy, appears to be exceedingly rare, as one would judge from the poverty of published reports, but in reality is probably more common, many cases having been overlooked at postmortem examination due to very small perforations. There is no doubt, however, that the incidence of perforation of an infarcted septum is much lower than that of rupture of the heart following infarction.

Mönckeberg [17] in a compilation of 39 cases of rupture of the heart by all causes found only three interventricular septum defects, a ratio of 1 to 13, and according to others, the ratio is even much lower. This fact is explained by the rich blood-circulation with which the lower portion of the septum is endowed, since both major coronary arteries contribute to its supply, as demonstrated by Gross [18] by means of injection.

The common denominators for the diagnosis of a septal rupture of this variety are two: (1) coronary thrombosis followed by (2) the sudden appearance of a loud systolic murmur and palpable thrill. In all cases comprising this review, including our own, with the exception of the first case of Bickel and Mozer (which the authors relegated to the "silent type"), there was a loud systolic murmur, most frequently heard best to the left of the sternum in the fourth and fifth interspaces. The absence of the murmur in Bickel's case may have been due to weakness of cardiac contractions. This location is in contrast to that of the murmur found in the congenital form, which is usually higher over the heart. It has been stated by Sager and others that the intensity of the murmur and thrill depends on the size of the aperture, the smaller the opening, the louder the murmur and the rougher the thrill. This review does not bear out such a conclusion.

The electrocardiographic findings which accompany this complication, in the majority of instances, do not differ from those characteristic of other cases of cardiac infarction, and depend on whether the involvement is greater in the anterior or posterior portions of the heart—the Q_1T_1 or Q_3T_3 type. It has been particularly noted that auriculoventricular conduction defects are rare. In only one case did the patient develop a complete block. The absence of conduction interference is accounted for by the fact that only a few twigs of conduction fibers are present in the apical portion of the septum; thus, its destruction has no influence on the electrocardiogram. However, in the cases of Gross and Schwartz and of Bayley, as well as in my

own, as the illness progressed, there was a change in the axis from normal to deviation to the right. With the clinical evidence of increasing right heart failure, the change in the axis deviation indicates augmented strain on the right side of the heart, similar to cor pulmonale, a finding which may be of aid in arriving at a correct diagnosis.

It appears from all reports that the addition of rupture of the septum to the presence of cardiac infarction makes the prognosis much more grave, although on theoretical considerations the cardiac dynamics should not be greatly affected. The intraventricular tension in the left ventricle being considerably greater than that in the right, the flow of blood, in the presence of an acquired interventricular aperture, is in the direction from left to right; thus, cyanosis is not an outstanding feature. What makes the outlook worse is the fact that the rupture of the septum is prima facie evidence of massive infarction of the myocardium. The duration of survival after the appearance of the murmur varies from a few days to several months. The patient of Gross and Schwartz lived five and one-half months after the murmur appeared, long enough to develop congestive failure. Stanley's patient died eight months after the beginning of her illness.

The size of the perforation varies from a pinpoint to 6 cm. There is usually only one communication, but in a few cases there were two or more.

In all the cases reviewed there was either complete occlusion of one or more of the major coronary arteries or marked narrowing of their lumina. In the majority of cases the left coronary artery was the one most severely affected, a fact which is consistent with the greater frequency of infarction of the anterior wall of the left ventricle. Evidence of atherosclerosis of the right coronary artery was also present in most cases. It is the opinion of most observers that although perforation of the septum usually follows thrombosis of the left coronary which supplies two-thirds of the septum, actual perforation does not take place unless the right coronary is also severely sclerosed and thus becomes incapable of supplementing, by way of anastomosis, the deficiency of the anterior coronary vessels. As was shown with special clarity by Blumgart et al.[19] multiple occlusions and narrowings of both coronary arteries are usually found in cases of massive infarction.

The diagnosis of this complication, as stated above, should not be difficult in most cases. A wider dissemination of the knowledge of the symptomatology which occurs when rupture of the septum follows coronary thrombosis should result in the more frequent recognition of this condition during life. One condition which may lead to difficulty in differential diagnosis is a sudden tear of a papillary muscle in the left ventricle. In that case, however, the clinical condition would show a more spectacular change for the worse than in the case of septal rupture, as one would expect to find the cardiac dynamics affected to a greater degree. The heart would dilate more rapidly and the clinical and electrocardiographic aspects would point toward greater failure of the left heart than of the right heart. The presence of relative tricuspid insufficiency as the result of weakness of the right ventricle may

lead to confusion in explanation of the systolic murmur, but in that case the murmur would be loudest over the xiphoid region rather than to the left of the sternum, and usually no thrill would be present. The history, electrocardiographic changes sufficient to make a diagnosis of cardiac infarction, and a suddenly appearing loud systolic murmur and thrill to the left of the sternum in the fourth and fifth interspaces make the diagnosis of ruptured septum most plausible.

Summary

1. An up-to-date review of the literature on perforated septum following cardiac infarction is presented and an additional case, diagnosed before death, is described.

2. Comments on the clinicopathologic syndrome are made.

I wish to thank Dr. W. J. Kerr for his generous assistance in the preparation of the illustrations.

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AMYLOIDOSIS COMPLICATING TUBERCULOSIS—DIAGNOSIS, PROGNOSIS AND TREATMENT*

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I. INTRODUCTION

THE substance, amyloid, is now considered to be a complex protein, the exact chemical composition of which has not yet been definitely determined. The disease, secondary amyloidosis, is looked upon by most contemporary observers as a disturbance of protein metabolism.

More effective treatment of syphilis and a more prompt surgical attack on suppurative foci have undoubtedly reduced these two common conditions as potential sources of amyloidosis and have served to center attention on tuberculosis as the chief current cause of this complication. The lesson is obvious. Early and adequate control of precavitary tuberculosis will prevent amyloidosis. The earlier and effective use of collapse therapy measures in advanced cases will minimize the development of amyloidosis. When the complication appears the prognosis is affected adversely. The advanced case of amyloidosis is a well known clinical picture and of academic interest only.

TABLE I

Incidence as to Race, Sex and Age

	Race		Sex		Age at Death	
	White	Colored	Male	Female	Youngest	Oldest
Number	63	16	43	36	14	67
Per Cent	80	20	54	46	66% of cases in age group between 20–39 yrs.	

The recognition of amyloidosis in its relatively early stage is of more importance and should stimulate reconsideration of methods for possible control of the underlying tuberculous lesion. Finally, there is the problem of active therapy directed toward the amyloidosis itself.

Material: This report briefly considers some features concerning the diagnosis, prognosis and treatment of amyloidosis. The study is based on a review of 79 patients who died of tuberculosis complicated by amyloidosis. The series is composed of: (*a*) Fifty-three cases in which the diagnosis of amyloidosis was proved by necropsy examination during a six year period ending January 1942. A total of 143 autopsies was performed and the incidence of amyloidosis was 39 per cent. (*b*) Twenty-six patients who, during life, had clinical evidence of amyloidosis and 100 per cent absorption

* Received for publication July 22, 1942.
From the Hudson County Tuberculosis Hospital, Dr. B. S. Pollak, Medical Director.

of the congo red dye but in whom necropsies were not done. These patients were observed between January 1939 and January 1942.

II. Diagnosis

A. Clinical Features:

1. The distribution of the cases as regards race, sex and age is presented in table 1.

2. The type of the underlying lesion in these patients can be summarized briefly as follows:

a. Pulmonary Tuberculosis: Seventy-seven or 97.4 per cent had progressive disease of varying degree with cavitation in one or both lungs. Many had also extrapulmonary involvement, particularly of the larynx and intestines. Only two patients, or 2.6 per cent, had arrested disease at the time of death.

b. Pleural Tuberculosis: Fifteen patients, or 19 per cent had an empyema (tuberculous or mixed); 13 were intrapleural and two extrapleural. By contrast, 8 of 88 autopsied non-amyloid patients, or 9 per cent, had an empyema. Thus, twice as many patients with empyema developed amyloidosis.

c. Major Surgical Operations: Six patients had thoracoplasty operations, three extrapleural pneumothoraces, and one patient both procedures. Two of the group were definitely known to have amyloidosis at the time of operation. Both died shortly after thoracoplasty, one with uremia, the other with a nephrotic syndrome.

d. Associated Non-Tuberculous Disease: One patient had a recurrent osteomyelitis of 16 years' duration, and another carcinoma of the pharynx and tongue. These conditions may have contributed to the development of amyloidosis.

3. *Hypertension:* Eight cases, or 10 per cent, of the group had hypertension.

4. *Hepatomegaly:* The liver was enlarged on physical examination in 46 cases, or 58 per cent; in the remainder, the liver was not felt on admission and no follow up notes were available. No instance of jaundice was seen.

5. *Splenomegaly:* The spleen was definitely palpable in 18 cases, or 22 per cent; no enlargement was found despite frequent examinations in 36, or 45 per cent; the spleen was not palpable on admission in the rest of the group and subsequent notations were not made.

6. *Clinical Status at Death:*

1. Causes not related to amyloidosis—intermittent complications such as profuse terminal hemoptysis, meningitis, etc., which interrupted the evolution of amyloidosis	15 cases, or 19 per cent
2. Progressive asthenia and no edema	23 cases, or 29 per cent
3. Slight to moderate edema	12 cases, or 15 per cent
4. Anasarca (including ascites)	24 cases, or 30 per cent
5. Uremia	5 cases, or 6 per cent

Dependent edema of the extremities in some instances was recurrent and not persistent. Once ascites set in, however, it tended to be persistent and the prognosis became graver. A complicating terminal pneumococcic peritonitis, seen frequently in non-amyloid nephrosis, did not occur in our series.

Amyloidosis is an insidious complication of tuberculosis. The commonest clinical signs are hepatomegaly and edema. Congestive heart failure must be excluded.

B. Laboratory Data:

1. *Blood:*

(*a*) *Anemia:* Sixty-seven of the 79 cases, or 85 per cent, presented anemia of varying degree.

(*b*) *Blood Chemistry:* Repeated determinations were usually made at three to four month intervals and very rarely longer than six months.

(*a*) Plasma protein determinations done in 49 cases showed decreased total protein and albumin in 53 per cent, hyperglobulinemia in 24 per cent, and a decreased or inverted A–G ratio in 63 per cent.

(*b*) In 10 out of 53 cases, or 19 per cent, the nitrogen values were above normal.

(*c*) Fifty-two per cent of a group of 40 showed a hypercholesteremia.

These figures represent the average pattern. Normal values may occur intermittently. The commonest laboratory findings in amyloidosis are decreased plasma proteins, A–G ratio, and elevated blood cholesterol.

2. *Renal Function Tests and Urinary Findings:*

Two kidney function tests were repeated with other clinical and laboratory studies.

(*a*) The renal concentration test was done in 50 cases and poor concentration was noted in 41, or 85 per cent.

(*b*) The phenolsulfonphthalein intravenous excretion test was performed in 38 cases and poor elimination of the dye was observed in 20, or 52 per cent.

We found the concentration test a better index of renal function in our amyloid cases.

Routine Examination of the Urine: A review of the urine examinations in the 53 autopsied cases and in a control group of 88 autopsied tuberculous cases who did not have amyloidosis (five of the latter had no urine examinations so that the estimate is based on 83 cases) was undertaken. The heat and acetic acid test was uniformly used to detect albuminuria by which we mean the presence of albumin of one plus or more in one or more specimens. By casts we mean the presence of hyaline or granular casts (many, few, occasional) in one or more samples of urine. In the vast majority of instances, the casts were hyaline only.

The very significant fact gleaned from table 2 is that 74 per cent of all the tuberculous patients who had proteinuria with casts were in the amyloid category. A checkup of the anatomical distribution of amyloidosis in the 53 cases revealed that 45, or 85 per cent, showed renal involvement. All of the 37 cases with albuminuria plus casts, or 82 per cent of the total affected kidneys, had amyloidosis. In four of the remaining eight cases minimal amyloid disease of the kidney was present; in three of these the urine was normal, whereas the fourth had albuminuria alone. Four other patients had moderate to marked renal amyloidosis. One patient had albuminuria, whereas three had negative findings and the time intervals between the last urine examination and dates of death were five and one-half months, five months and six weeks. It is possible that in at least two of these patients, study of the urine closer to death might have revealed positive findings.

TABLE II

Urinary Abnormalities in Autopsied Cases

Urinary Findings	Autopsied Amyloid Cases	Autopsied Non-Amyloid Cases	Total = 136 Cases	
	No.	No.	No.	%
Albumin only	5	20	25	18.3
Casts only	0	2	2	1.4
Albumin + Casts	37	13	50	36.7
Negative Urine	11	48	59	43.3

Note: In the clinically diagnosed (non-autopsied) group of 26 cases, 21, or 80.8 per cent, had albuminuria and casts and five, or 19.2 per cent, albuminuria alone.

In the non-amyloid group, there were 35 patients with abnormal urinary findings and the most frequent specific renal disease among them was tuberculosis.

The commonest urinary signs in amyloidosis are albumin and casts. Their presence, even in the absence of other confirmatory data, strongly indicates amyloidosis provided tuberculosis of the kidney is excluded.

Congo Red Test: Bennhold (1923) [1] devised this test for the detection of amyloidosis. He believed that a positive test was one in which 60 per cent or more of the dye disappeared from the blood stream at the end of one hour. A negative test, he felt, does not rule out amyloidosis for small localized deposits especially in the kidneys alone may not be sufficient to give the typical result.

There is unanimity of opinion that 100 per cent elimination of the dye at the end of one hour is diagnostic of amyloidosis. However, this simply adds laboratory confirmation to what is already quite evident from a clinical standpoint in the majority of tuberculous cases, as indicating amyloidosis.

The Congo red test would be of more value if it enabled one to detect early cases of amyloidosis. Can it do so? In an attempt to answer this, we sought to determine first the rate of elimination of the dye from the blood

stream in normal individuals. Tests were performed in 25 cases. Regardless of body weight, each received 10 c.c. of a 1 per cent aqueous solution of congo red intravenously. Samples of blood were removed four minutes, one hour, two hours and four hours after injection. At the end of one hour, the minimum per cent of the dye removed from the blood was 14, the maximum 53 and the average 29.5. At the end of two hours, the comparable figures respectively were 17, 57 and 44.5. All but a trace of the congo red was eliminated at the end of four hours in all of the cases. A curve of the rate of disappearance of the dye, representing average values, is shown in figure 1. Thus, the average excretion of the dye in normals at the end of

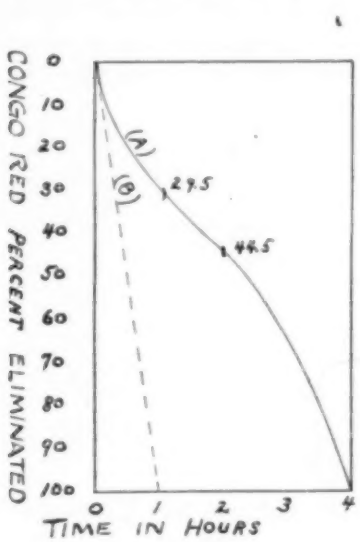

Fig. 1.

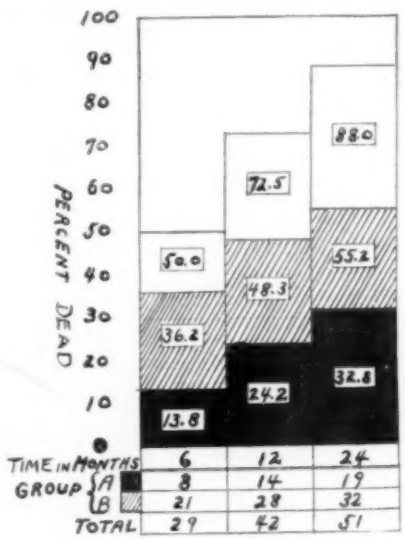

Fig. 2.

FIG. 1. Elimination of congo red from blood. A—Average curve in normals. B—Typical curve in amyloid cases.

FIG. 2. Duration of illness from abnormal urinary findings to death. Group A—clinically diagnosed cases. Group B—autopsied cases.

one hour is about one-third that of the definite case of amyloidosis. In fact, we have noted that some amyloid patients may absorb all of the dye in considerably less than one hour. We believe that 60 per cent removal from the blood is suggestive of amyloidosis but 100 per cent is diagnostic. We also believe that the test has definite limitations, because it is very difficult, according to our experience, to make accurate colorimetric observations in the intermediate zone between 60 per cent and 100 per cent. This impairs its usefulness for the diagnosis of early amyloidosis.

Next, we wish to refer briefly to some technical aspects of the test.

(1) How often can the test be repeated?

In a group of eight amyloid cases with 100 per cent dye retention, the congo red injection was repeated daily or every other day for several days

and in each case, 100 per cent absorption persisted. No toxic or cumulative effect was noted. We do not know what the saturation point is, if any, with congo red.

(2) One of the most important sources of error is the presence of hemolysis. To avoid this, we have resorted to the following:

(*a*) The use of an absolutely dry syringe and a large caliber needle.
(*b*) Heparin as the anticoagulant (Gerber and Fryczynski [2]).
(*c*) Prompt centrifugation of specimens. If, despite precautions, hemolysis occurs, the test is repeated in one or two days.

(3) In many cases, simultaneous determinations with the Bennhold and acetone technic (Friedman and Auerbach [3]) were made. The latter gave a consistently higher percentage of withdrawal of the dye from the blood; the acetone definitely "takes up" some of the dye. All but one of the congo red results mentioned in this paper were reported according to the Bennhold method.

Sixty-two of the 79 patients had congo red tests performed at intervals. These patients can be divided into two groups:

Group A: With 100 per cent retention of the dye in one hour—37 cases or 60 per cent. Thirty-two had albuminuria and casts, and in 12, or 35 per cent, these urinary findings antedated the first positive congo red test. This was so significant from the point of view of early diagnosis that the same aspect was investigated in a group of 22 living amyloid cases. Proteinuria and casts preceded the first positive dye test in seven cases, or 31 per cent, and corroborated closely the above mentioned percentage.

Group B: Less than 100 per cent retention—25 cases (autopsied) or 40 per cent. Eighteen patients had albuminuria and casts. Thus it is seen that the examination of the urine could have furnished a better clue for the diagnosis of amyloidosis than the congo red test. Why did the test fail in this group? In 10 instances, it was done three months or more before death so that failure may have been due in part at least to the prolonged interval that elapsed. In 15 cases, the test was performed within a three month interval preceding death; three of these showed only minimal hepatic involvement and the remaining 12 cases had moderate to marked hepatic and multiple organ amyloidosis. The possibility of faulty technic in the performance of the test in this group should be considered.

III. Prognosis

We believe that one of the best single objective findings in the early diagnosis of amyloidosis in a tuberculous subject is the presence, at first intermittently and later more persistently, of albumin and casts. Examination of the urine is a simple and universally used test, and although the above criteria are not a perfect guide, they are probably the least imperfect except

for 100 per cent congo red retention. However, the value of the latter is somewhat dissipated not only by the fact that it is a special test requiring careful technic but also because, from our material, albuminuria and casts antedated 100 per cent dye absorption in about one-third of the cases.

We, therefore, suggest that the onset of the abnormal urinary signs mentioned above may be used with a reasonable degree of assurance to indicate the approximate detectable onset of amyloidosis. With this yardstick, one

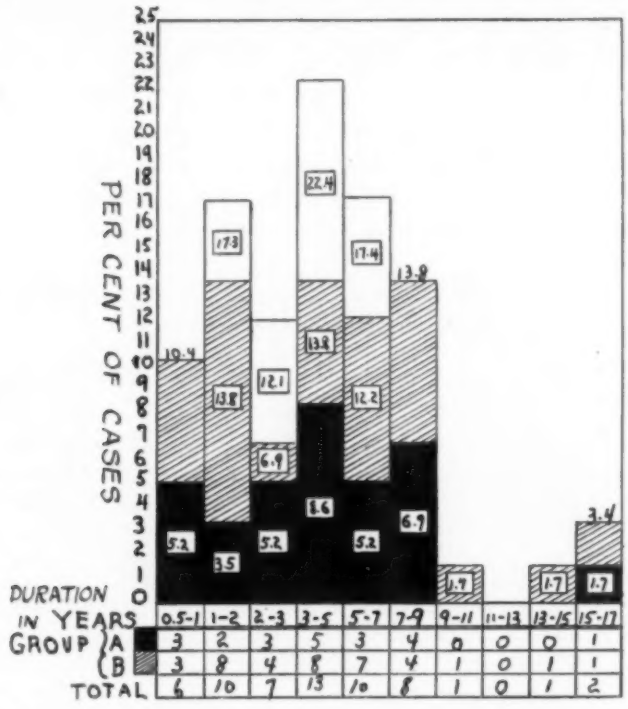

FIG. 3. Duration of illness from clinical onset of tuberculosis to abnormal urinary findings. Group A—clinically diagnosed cases. Group B—autopsied cases.

may then attempt to reconstruct the life cycle of these patients by dividing the duration of illness into two phases:

(1) from the clinical onset of tuberculosis to the onset of albuminuria and casts, and

(2) from the onset of these abnormal urinary findings (or amyloidosis) to death. The data in figures 2 and 3 are based on 58 cases of the entire group who had proteinuria and casts. The average total duration was 64.2 months. In the first period of illness, the average duration was 51.8 months, the minimum six months and the maximum 17 years. In the second phase, the average length of life was 12.4 months; 50 per cent of the patients died within the first six months, another 23 per cent in the next six months and an additional 15 per cent between the first and second years. In other words, 51

cases, or 88 per cent, were dead within two years after the development of amyloidosis. (This compares very closely with the 92 per cent mortality at the end of the same time interval reported by Pearlman.[4]) The estimated duration of amyloidosis in one of the remaining seven cases was as long as 10 years. This patient had arrested tuberculosis and died from uremia. It should be emphasized again that this recapitulation is only an approximate time table but nevertheless an enlightening one from a prognostic viewpoint. The prognosis in amyloidosis is greatly affected by the character and extent of the underlying tuberculous lesion.

IV. Treatment

Secondary amyloidosis has continued to be mainly a disease of diagnostic interest. Relatively little has been written about its treatment. As mentioned at the outset, the most important factor in the treatment is prevention. However, once amyloidosis develops, what therapy, if any, can be employed?

Before presenting our personal experiences, brief reference to some of the experimental and clinical reports pertaining to the treatment and reversibility of amyloidosis is warranted. Kuczynski [5] and later Morgenstern,[6] among others, noted resorption of amyloid in mice after injections of sodium caseinate were stopped, provided the lesion was not too far advanced. The latter author found some connective tissue replacement in the liver. Grayzel et al.[7] showed that a proper diet with an abundance of vitamins A and B would retard the production of amyloidosis in mice. Furthermore, the oral use of powdered whole liver produced resorption of moderate deposits of amyloid. Jaffé [8] noted that amyloidosis was prevented when cholesterol supplemented the stock diet. Letterer [9] found that amyloidosis developed more rapidly in animals whose water intake was restricted.

Gairdner [10] and Walker [11] each reported a case of regression of the clinical signs of amyloidosis. One followed amputation of a leg as the result of osteomyelitis, the other after obliteration of a chronic empyema by thoracoplasty. Reimann [12] reported the status of a patient with a controlled tuberculous lesion three years after thoracoplasty in whom clinical recovery was noted. Métraux [13] mentioned an interesting case of clinical recession which revealed slight anatomical healing in the liver only on autopsy examination. Habein [14] and Rosenblatt [15] also reported single cases of amyloid regression. Pearlman [16] similarly described four cases from a clinical point of view. Waldenström [17] reported punch biopsy studies of the amyloid liver with reversal in three cases after the healing of bone tuberculosis. Snapper and Ch'in [18] speculate on the influence of diet in amyloidosis. They mention its very low autopsy incidence (1.3 per cent) at the Peiping Union Medical College. The complete absence of dairy products and foods with high casein content from the diets of the population in Northern China may be an important factor in the infrequency of amyloidosis. Whitbeck [19] gave powdered whole liver (12 grams daily) over a period of two years to seven chil-

dren who were treated for bone and joint tuberculosis. After 18 months it was noted in five cases that the spleen and liver receded, albuminuria and edema disappeared, although the congo red test was still positive. This short review of the literature indicates:

(*a*) that experimentally induced amyloidosis of moderate degree may recede spontaneously after the causative irritant is removed;

(*b*) that there is clinical evidence in man of amyloid regression after control of the basic pathological condition is accomplished. Definite anatomical proof of regression is not yet convincing;

(*c*) that proper diet supplemented by a liberal intake of vitamins and liver may perhaps be of some value in the treatment of amyloidosis. This assumption stimulated the therapy phase of our study.

A. Material: The following report is concerned with 30 cases which had at least six months of treatment up to January 1942. Necessary treatment for tuberculosis was carried on pari passu. The group of 30 comprises 13 patients who are dead and included in the original series of 79 and in addition 17 living amyloid patients, eight of whom were still in the hospital and nine of whom were attending the out patient clinic.

B. Duration of Amyloidosis: The average span of life during the amyloid phase (computed to date of death, in living patients to January 1942) (table 3) was greater than the average duration noted in figure 2, but we

TABLE III

Duration of Amyloidosis

Treated Cases	Average	Minimum	Maximum
Dead (13)	20.2 mos.	6 mos.	6 yrs.
Living (Hosp.) (8)	20.1 mos.	7 mos.	3 yrs.
Living (O.P.D.) (9)	28.2 mos.	15 mos.	3 yrs.

cannot honestly state at this time that this increase was due to the therapy for amyloidosis alone.

C. Type of Underlying Tuberculosis: This must be considered in evaluating the results of treatment. The lesions have been classified as noted in table 4.

TABLE IV

Type of Pulmonary Lesion

Treated Cases	Slowly Progressive		Quiescent	Arrested	Empyema	Major Surgery	
	Mainly Unilateral	Mainly Bilateral				Thoracopl.	Extrapl. Pnx.
Dead (13)	2	11	0	0	3	3	1
Living (Hosp.) (8)	3	3	3	0	2	1	0
Living (O.P.D.) (9)	1	0	3	5	1	2	1

D. Treatment: 1. *Duration:* The period of treatment ranged from six to 36 months (table 5). 2. *Type:* Twenty-three patients received a combination of oral and parenteral therapy, whereas seven had medication by the former route alone (table 5). The basic oral therapy was as follows:

(*a*) high protein diet which is very important because of albuminuria;
(*b*) iron in the form of feosol, 9 to 12 grains daily for secondary anemia;
(*c*) dilute hydrochloric acid (90 minims daily). Gastric analyses were done in 28 patients of whom all but one showed either an achlorhydria or hypochlorhydria. No reappearance of free acid was noted in the former

TABLE V
Treatment

	Duration			Type		Results		
	Average	Minimum	Maximum	Parenteral	Oral Alone	Decreased Liver	Normal Urine	Normal Congo Test
Dead (13)	11.7 mos.	6 mos.	3 yrs.	11	2	0	0	0
Living (Hosp.) (8)	16.7 mos.	6 mos.	32 mos.	4	4	0	0	0
Living (O.P.D.) (9)	22 mos.	12 mos.	33 mos.	8	1	3	1	1

group. All had smooth tongues with varying degrees of papillary atrophy and three had associated glossitis. It has been shown that the gastric juice is normally an important element in the extraction of iron and vitamins from their natural food products (Sydenstricker [20]) Achlorhydria is common in all deficiency diseases and is believed to be a specific effect of nicotinic acid deficiency. In the three patients with glossitis, two received nicotinic acid (15 to 20 mg. daily for several days) and the third, amino acids intravenously which contain liberal amounts of nicotinic acid. All showed practically complete disappearance of the glossitis with marked improvement in the gross appearance of the tongue. These patients may have been suffering from a chronic deficiency (partial or complete) of the B vitamins which may be due not necessarily to an inadequate intake but rather to poor absorption and utilization of vitamins. The triad of anemia, lingual changes and depressed function of the gastric mucosa is commonly seen, of course, in non-amyloid tuberculous patients; but attempts at its correction were made on the assumption that amyloidosis which in itself is presumed to result from disordered metabolism might be benefited indirectly.

Supplemental parenteral therapy was given to 23 patients, 21 receiving liver extract, and two thiamin chloride. The former was used empirically, largely on the basis of the reports described above. The Lilly product was employed, each cubic centimeter containing 2 U.S.P. units which is equivalent to 25.5 grams of fresh powdered liver. The average dose was two cubic centimeters twice weekly (intramuscularly) during the hospital

stay and once weekly to out patient cases. It was difficult to determine a definite maintenance dose. Since one may justifiably suspect impaired absorptive capacity of some of the nutritional requirements in these patients, especially in the presence of intestinal tuberculosis, it was felt that parenteral liver therapy might be expected to yield better results (if any at all were to be obtained) than its oral administration. In five cases, thiamin chloride (2 c.c.) was added to each dose of liver extract. Seven patients who refused the injection therapy received vitamins and betaxin by mouth.

With the appearance of edema in 14 patients, treatment was augmented by the restriction of fluid intake, salt poor diet and diuretics when necessary. Considerable but usually temporary diuresis was obtained with ammonium chloride and salyrgan or mercupurin. In a patient, however, with kidneys damaged by amyloid, the repeated use of a mercurial compound would seem like adding insult to injury. One patient with intestinal ulceration had a bloody stool on three occasions after several courses of mercury.

3. *Results:* The following were the chief criteria employed in evaluating the effects of therapy (table 5):

(*a*) significant reduction in size of liver or spleen;
(*b*) disappearance of albumin and casts;
(*c*) conversion from a positive to a negative congo red test confirmed by repeated injections.

In the dead and living hospitalized cases, there appeared to have been no dramatic or essentially basic improvement in the amyloid status. Reduction in edema, increased hemoglobin, elevated plasma protein level and better appetite were beneficial signs temporarily noticed in some. Whether the therapy may have tended to retard progression of the amyloidosis, we cannot say. Four of the living out-patient cases, however, showed definite objective improvement. Conversion to a normal congo red test was noted in one, reduction in the size of the liver in three with disappearance of proteinuria and casts in one of these. Moderate edema was present in one case for many weeks but has not recurred in more than two years. Plasma protein and cholesterol were maintained within normal limits. Liver extract was used in two cases and thiamin chloride alone in the remaining two. The duration of treatment in these cases ranged between 24 and 28 months.

How great a rôle the treatment actually played in producing these changes is difficult to state. The dominant element may well have been the fact that the underlying tuberculosis was in the process of being controlled when therapy was started and later became arrested. It is possible that these cases may have shown signs of clinical regression without any treatment whatsoever.

Postmortem examination in five of the 13 patients who died showed no definite evidence of anatomical regression of amyloidosis, including one patient who received liver extract (6 c.c. weekly) for a period of three years.

Treatment of amyloidosis, as outlined above, in the presence of uncontrolled tuberculosis is uniformly disappointing. Adequate control of tuberculosis is a necessary prerequisite for better results. Treatment with proper diet, vitamins and liver extract may perhaps be of some value in combating amyloidosis in a select group of tuberculous patients in whom the basic disease is inactive or in whom there is at least a reasonable chance that it will become so in a relatively short time.

V. Summary

A. Amyloidosis is a common complication of tuberculosis. The incidence in a group of 143 autopsied patients was 39 per cent.

B. A series of 79 cases of amyloidosis, which comprised 53 autopsied patients and 26 clinically diagnosed patients (nonautopsied) with 100 per cent congo red retention, is reviewed. Interesting clinical features are briefly presented. Significant laboratory findings and correlative studies are mentioned. A checkup of the urine examinations in 143 autopsied tuberculous cases was made; about 75 per cent of those who spilled albumin plus casts had amyloidosis. This is emphasized as a diagnostic criterion. Several aspects of the interpretation and technic of the congo red test are discussed. One hundred per cent absorption of the dye by the tissues, within one hour, is indicative of amyloidosis. A negative congo red test, however, does not exclude amyloid disease. Albuminuria and casts antedated 100 per cent congo red retention in about one-third of a group of 37 cases.

C. Charts are presented in an attempt to visualize the prognosis of 58 tuberculous patients, with amyloidosis, using the above urinary findings as connoting the probable "onset" of amyloidosis. According to this compilation, almost 90 per cent were dead within two years after the development of amyloidosis. The nature of the underlying tuberculous lesion greatly influences the span of life in the amyloid phase.

D. The status of 30 patients who received treatment for six months to three years for amyloidosis is reviewed. The basic oral therapy was a high protein diet, iron and dilute hydrochloric acid. Twenty-three also received parenteral therapy which was chiefly liver extract. Definite objective improvement in the amyloid status was found in four patients who had arrested tuberculous disease. Adequate control of tuberculosis was probably the chief factor in the improvement noted. There was no evidence of anatomical regression of amyloidosis in five autopsied cases.

I wish to express my appreciation to Dr. I. E. Gerber, Pathologist and Director of the Laboratory, Hudson County Tuberculosis Hospital, for his helpful suggestions.

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CASE REPORTS

LIGATION OF A PATENT DUCTUS ARTERIOSUS WITH PROBABLE ENDARTERITIS; APPARENT CURE*

By J. W. Nixon, M.D., F.A.C.S., W. W. Bondurant, Jr., M.D., F.A.C.P., and Omer Roan, M.D., F.A.C.S., *San Antonio, Texas*

Unusual consideration is now being given in America to the surgical treatment of patent ductus arteriosus. One of us (Nixon) has recently reviewed the surgical aspects of the disease. Since the report of Touroff et al. of the cure of three cases of subacute *Streptococcus viridans* endarteritis following the successful surgical ligation of a patent ductus arteriosus, renewed interest has been shown in subacute endarteritis of this type. Their work definitely extends the benefit of surgical ligation of patent ductus arteriosus by offering a possible cure of this very serious complication. The report of an additional case successfully treated by operative means in which a sterile blood culture was obtained within a few minutes after the duct was ligated, therefore, seems warranted.

Case Report

L. B., a white girl, aged nine, weight 56 pounds, was a full term child. Delivery was normal. There was no evidence of heart disease at birth. She had whooping cough at the age of three, but no other childhood diseases. At the age of six, upon entering school, a heart murmur was found by the school physician. Her tonsils were removed at that time. Her activity was not limited and her course in school was uneventful until December 1941, at which time she developed mumps. She returned to school after this attack and was in good health until January 16, 1942. At this time she developed a febrile illness with upper respiratory symptoms, thought to be influenza. Her temperature the first two days ranged as high as 104° F., and following this moderately severe infection she continued to have fever daily, the peaks ranging between 99° F. and 102° F. The same heart murmur which had been noted three years previously was still present. Until February 14, 1942, she was treated with various sulfonamide drugs without any evidence of improvement. On this date a roentgenogram was made which showed very slight prominence of the pulmonary conus (figure 1). A blood culture showed the presence of numerous colonies of *Streptococcus viridans*. On February 18, 1942, she was admitted to the Nix Hospital. When examined on this date the child showed considerable pallor. Blood pressure was 122 mm. Hg systolic and 72 mm. diastolic, pulse 116, temperature 100.2° F. Her heart was not enlarged. There was a loud continuous murmur heard best in the second left interspace about 6 cm. to the left of the midsternal line. The murmur waxed in intensity during systole and waned during diastole. It was typically machinery-like. The systolic component of this murmur was heard over the entire precordium, but was much softer. No thrill could be felt. The chest was clear. The spleen was definitely palpable, extending with deep inspiration two fingers' breadth below the left costal margin. There were three small areas on the hands and

* Received for publication August 11, 1942.

fingers about 2 mm. in diameter which were bluish-red in color and apparently were the result of tiny emboli.

The urine varied in specific gravity from 1.009 to 1.022 and contained a trace of albumin, a few pus cells, an occasional hyaline and granular cast, and no red blood cells. The blood counts were as follows: February 18, 1942—Hemoglobin 72 per cent, red blood cells 4.56, white blood cells 6,980; differential: nonsegmented neutrophiles 6, segmented 61, lymphocytes 22, eosinophiles 6, monocytes 5. After several transfusions, on February 21, 1942 the blood count was as follows: Hemo-

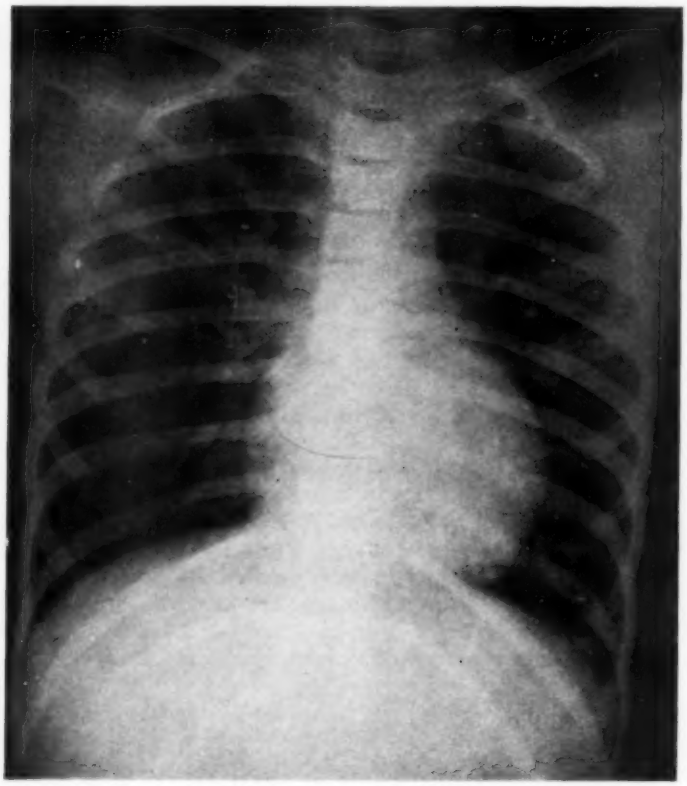

FIG. 1. Roentgenogram of heart before operation.

globin 79 per cent, red blood cells 4.48, white blood cells 9,000; differential: nonsegmented neutrophiles 20, segmented 61, lymphocytes 13, monocytes 6. Blood cultures on February 18, 1942 and February 24, 1942 showed *Streptococcus viridans* in large numbers occurring in pairs and short chains. Her temperature showed an evening rise to 102° F., and in the morning varied between 99° and 99.8° F. Her pulse ranged between 110 and 140, respirations between 22 and 24. The diagnosis at this time was patent ductus arteriosus, *Streptococcus viridans* septicemia, *Streptococcus viridans* endarteritis. Sulfapyridine was administered in adequate doses for about 10 days with no effect on the temperature or pulse, then sulfadiazine was substituted. On March 17, 1942 the blood sulfadiazine concentration was 7.3 mg. per cent, the CO_2 combining power 49.3 volumes per cent. A blood culture at the same time showed a heavy growth of non-hemolytic streptococci and occasional colonies

of staphylococci. These latter were considered by the laboratory to be possibly a contaminant.

On March 24, 1942 an electrocardiogram was made (figure 2). The rate was 107, sinus rhythm, P–R 0.16, QRS 0.05. The electrical axis was plus 90.

Ligation of the patent ductus arteriosus had been urged since the middle of February. Inasmuch as she had shown no improvement, operation was finally agreed to and on April 13, 1942 she was admitted to the Santa Rosa Hospital. Her temperature was 100° F., pulse 140, respirations 26, and blood pressure 110 mm. Hg systolic and 70 mm. diastolic. The physical findings were the same as before. A blood culture on that day was positive for *Streptococcus viridans*.

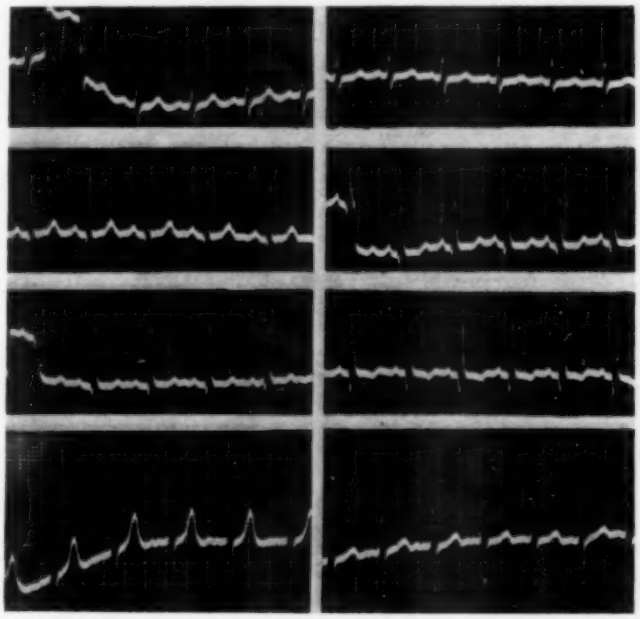

FIG. 2. Electrocardiogram before operation.

Operation: The patient was operated on April 14, 1942. She was placed on her back with a small pillow under the left shoulder, and with the left arm placed above her head. Cyclopropane anesthesia was administered by the intratracheal method. An incision was made on the left side of the chest, beginning at the lateral border of the sternum and extending laterally to the anterior axillary line over the right second costal interspace. The skin was incised, and the pectoralis muscles were cut in the line of the skin incision. The cartilages of the second and third ribs were cut just medial to the costo-cartilage junction. The pleural cavity was opened through the second interspace. The lung was collapsed and retracted posteriorly and downward, exposing the pericardium and mediastinum, along which could be seen coursing the phrenic nerve. The mediastinal pleura was picked up gently with fine forceps and was opened through an incision about two inches in length, beginning at the base of the lung and extending upward toward the neck. The fatty areolar tissue was carefully dissected away, exposing the pulmonary artery and the aortic arch. The thrill at its maximum was found to be over a vessel which extended from the pulmonary artery to the aortic arch, entering the aorta just opposite the left subclavian

artery. This structure was one and one-half centimeters in diameter and about two and one-half centimeters in length. It was carefully freed from the surrounding tissues by blunt dissection until the anterior, medial and lateral surfaces were freed and thoroughly exposed. A large aneurysm needle was carefully passed under this structure, separating it from the right bronchus. The lumen of this vessel was closed by traction on the silk which had been placed around it, and the condition of the patient was observed for a period of four or five minutes.

During the time that the vessel was held closed, the patient exhibited no untoward symptoms but the thrill disappeared as well as the murmur to which one of us (Bondurant) was listening through a sterile stethoscope. The diastolic blood pres-

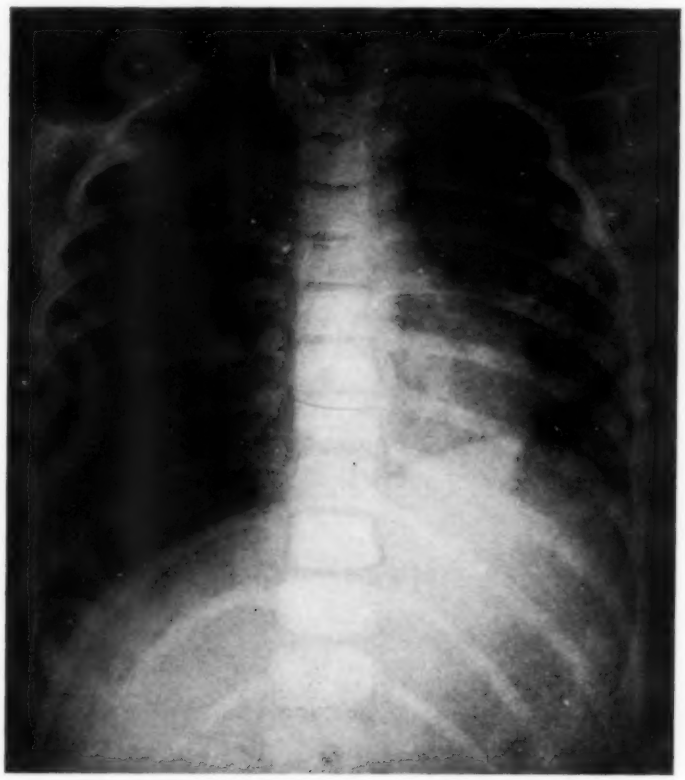

FIG. 3. Roentgenogram of chest after operation.

sure, which had been 60 to 70 mm. Hg, rose to 90 mm. The pulse slowed somewhat. It was felt this was sufficient evidence to prove that the structure with which we were dealing was the ductus arteriosus, and it was accordingly doubly ligated with number eight braided silk. A small amount of oozing was encountered in the region of the recurrent laryngeal nerve, but this was controlled by pressure with moist gauze. No effort was made to close the mediastinal pleura because it was felt that if any oozing should occur it would be better to have it enter the thorax rather than to be held in the mediastinum. The lung was then inflated by positive pressure. The cartilage was sutured with No. 32 annealed wire. Two lengths of size No. 30 wire were passed around the second and third ribs, pulling them into apposition with each other. With continuous No. 1 chromic catgut locked sutures, the soft tissues were closed. The skin was closed with a continuous lock silk suture.

Postoperative Course: The patient was not shocked following the operation. She was placed in an oxygen tent only as a routine procedure in operations on chest cases. On the second postoperative day, 350 c.c. of blood-tinged fluid were removed from the left side of the chest. She was discharged from the hospital on the seventh postoperative day.

The patient was examined soon after the operation. There were no murmurs heard over the precordium nor over the pulmonary conus. On the second postoperative day the pulse was 120 and blood pressure 120 mm. Hg systolic and 102 mm. diastolic.

Four blood cultures were taken postoperatively and all were sterile. The first of these sterile cultures was taken 22 minutes after the duct was ligated. The second was taken three hours later, the third on the second postoperative day, and the last one on the day of her discharge from the hospital, April 20, 1942.

Temperature in the hospital ranged from 99.6° to 102.6° F. It was below 100° the last two days of her hospital stay, reached 100° her first day at home, and following that was continuously no more than 99°. Practically every afternoon and evening her temperature was 99°. Her pulse in the last few weeks was between 86 and 92. She has received none of the sulfonamides since the operation.

On May 20, 1942 the patient was again examined. Her blood pressure was 114 mm. Hg systolic and 80 mm. diastolic. Her appetite was good and she had gained some weight. She felt quite well. The heart was normal. The spleen could not be felt. A blood culture was attempted but because of previous punctures and venous thromboses the veins could not be entered. A roentgenogram of the chest (figure 3) showed an elevation of the left side of the diaphragm, probably from injury to the phrenic nerve by retraction. In the area of the pulmonary conus there was a concavity to the left. An electrocardiogram (figure 2) on this date showed an inversion of the T-wave in Lead III, and a Q-wave in Lead III. Some of the changes, both in the electrocardiogram and in the cardiac silhouette, were thought to be due to the considerable elevation of the left side of the diaphragm and consequent displacement of the heart.

Summary

1. A case of patent ductus arteriosus with repeatedly positive blood cultures showing *Streptococcus viridans* is reported in some detail.

2. Sulfonamide therapy had no effect on the blood stream infection.

3. Ligation of the ductus arteriosus resulted in an almost immediate disappearance of the streptococci from the blood stream.

4. Although only five weeks had elapsed since the operation, and it was too early to make a definite statement, a cure seems to have been effected.

Addendum (November 12, 1943). Twenty months after the operation the patient has entirely recovered. She has had no elevation in her temperature above normal. No heart murmur is present, and she has gained twenty-eight pounds. She attends school where she takes part in light athletic games. One of us (Roan) removed a gangrenous appendix for her one year ago. Her recovery from that operation was uneventful.

MONOCYTIC LEUKEMIA ASSOCIATED WITH BONE CHANGES *

By ROBERT J. KOSITCHEK, M.D., *Los Angeles, California*

THE purpose of this paper is to present a case of monocytic leukemia which demonstrates the bone involvement previously observed in the lymphocytic and myelogenous types of leukemia. A review of the literature has failed to reveal similar bone involvement in leukemias in which the dominant cell is a monocyte or one of its immature forms.

Numerous accounts of bone changes in leukemia have appeared in the literature. In 1878, Newman and Eisenlohr [5] described pathological changes in the bones in leukemia. Subsequent reports of bone changes in myelogenous and lymphatic leukemia were made by Osler,[19] Snelling and Brown,[23] Doub and Hartman,[8] Poynton and Lightwood,[20] Karelitz,[14] Ewing,[12] Karshur,[15] Smith,[22] Ehrlich and Fover,[10] Baty and Vogt,[1] Clark,[2] Conybeare,[5] Connor,[1] and Craver and Copeland.[6]

In the case reports of monocytic leukemia by Reschad and Schilling-Torgau,[21] Dameshek,[7] Osgood,[18] Evensen and Schartum-Hansen,[11] Klumpp and Evans,[16] Jetter,[13] and in the reviews by Clough [3] and Osgood,[17, 18] no mention is made of bone changes.

CASE REPORT

R. P., male, aged 19, entered the Simpson Memorial Institute on September 28, 1938. The predominating symptoms were pain and limitation of motion in the right arm and shoulder, pain and weakness in both hips and thighs. The onset of the present illness was in May 1937, at which time the patient suffered from an upper respiratory infection. Physical examination at this time revealed a swelling in the upper left quadrant due to a very much enlarged spleen which practically filled the entire abdominal cavity. The white blood cell count was 307,200 per cubic millimeter.

The patient had one severe attack of epistaxis in May 1938. In September 1938, pain, dull aching and throbbing in type, appeared in both thighs and radiated anteriorly and posteriorly down to the knee. The patient experienced difficulty in walking, and was obliged to stiffen his knees when attempting to walk in a straight line. The pain became so severe that sleep was impossible without sedation.

The pain in the thighs was present on the day of admission, and the same type of pain was also present in the right shoulder with a resultant discomfort and limitation of motion. There had been a 10 pound weight loss in the previous three months.

During the 16 months that the patient was under observation before admission, his treatment consisted of ferric ammonium citrate, Fowler's solution, wheat germ oil, prontylin, Kinney's yeast extract, betalin, and Lilly's liver extract, and roentgen-ray therapy.

The patient had several courses of roentgen-ray therapy over the anterior, lateral, and posterior splenic ports, over the right and left axilla, right and left inguinal regions, and over both legs posteriorly. The dosage varied between 72 and 125 roentgen units and the time interval depended upon the patient's blood count and skin condition.

Physical examination revealed an emaciated, well developed adolescent male, subacutely ill, who appeared to be favoring a painful right shoulder. The patient walked with a shuffling, spastic gait, and the right shoulder was held in an "attention" attitude. The abdomen revealed an asymmetry with splenic and liver enlarge-

* Received for publication February 14, 1942.

ment. The spleen measured 21 cm. in the anterior axillary line, extending below the umbilicus on the left and 7.5 cm. to the right. The liver extended 6 cm. below the right costal margin. The liver and spleen were firm, smooth, non-tender, and freely movable. The upper extremities revealed limitation of motion of the right arm, but complete range of motion with passive exercise. Pressure over the right clavicle and shoulder elicited pain. The left arm was not abnormal. The lower extremities revealed pain and discomfort in the hips and thighs with movement. In order to bend the knees the patient first extended his legs and then pushed with his feet until proper leverage could be obtained. The patient was unable to move his legs rapidly or coördinate the movements. The reflexes were physiologic in the upper extremities; there was a loss of knee reflexes with normal plantar and Achilles

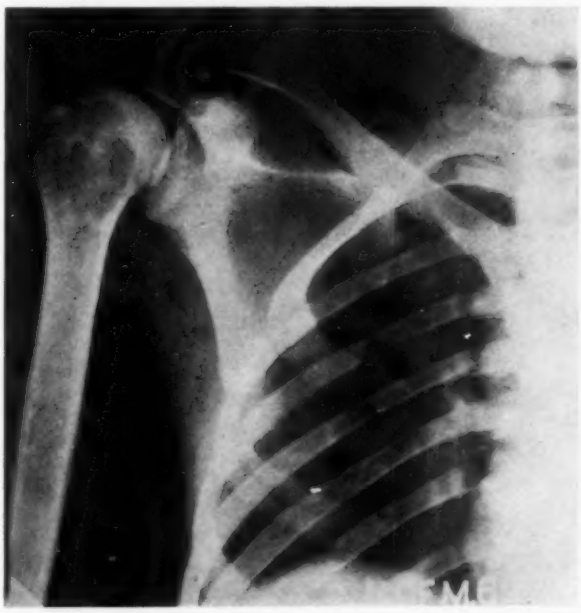

FIG. 1. Lesions present in the region of the surgical neck of the humerus. The lesions are osteolytic in character and involve the medullary portion of the bone. Calcium withdrawal from right clavicle with cystic formation.

reflexes in the lower extremities. A complete neurological examination of the upper and lower extremities revealed no definite evidence of nervous system disease and no evidence of peripheral neuritis.

Laboratory examination reports were as follows: The hemoglobin was 61 per cent (9.5 grams, Sahli). The red blood cell count was 3,250,000 per cubic millimeter; white blood cell count was 17,900 per cubic millimeter. The hematocrit was 28 per cent. Examination of a film stained with brilliant cresyl blue and Wright's stain revealed polymorphonuclear neutrophiles, adult, 33 per cent, young 16 per cent; metamyelocytes, 11 per cent; lymphocytes, 3 per cent; monocytes, adult, 3 per cent, young, 2 per cent; metamonoblasts, 21 per cent; non-classified blasts, 4 per cent; monocytoblasts, 2 per cent; eosinophiles, 3 per cent. The red blood cells appeared small. The platelets were increased in number. There was a mild basophilia of the neutrophiles.*

* Blood findings were substantiated by Drs. Raphael Isaacs and S. Milton Goldhamer of the Simpson Memorial Institute, Ann Arbor, Michigan.

Urine examination revealed no abnormalities. Bence-Jones protein was absent. The Kahn test for syphilis was negative. The stool examinations were negative for occult blood, ova, and parasites.

The roentgenographic report was as follows: Definite lesions were present in the region of the surgical neck of the humerus. These lesions were interpreted as osteolytic in character and involved the medullary portion of the bone. Less extensive changes were noted in the upper third of the femur proper—these changes might be due to osteoporosis. Osteoclastic changes were also noted in the right clavicle. In addition, it was noted that there was withdrawal of calcium in the medial portion of

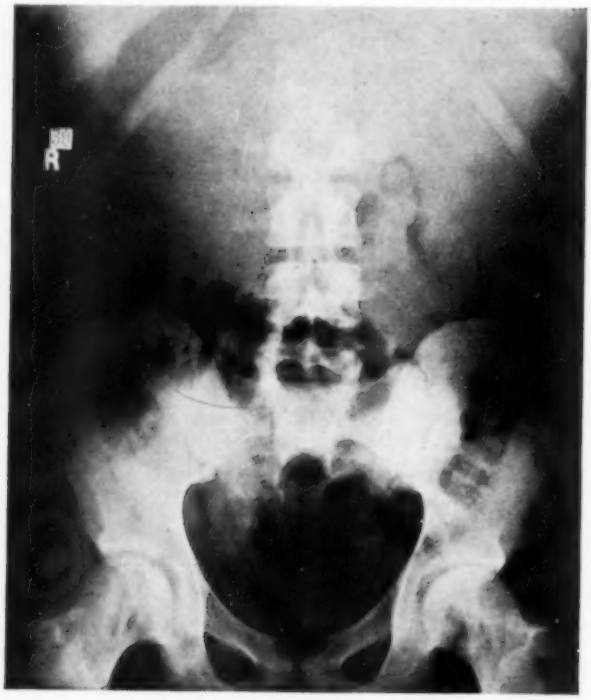

FIG. 2. Circular areas of bone destruction in each ischium and about the right acetabulum. Suggestive changes in the iliac portion of the left acetabulum. A destructive process on the lateral margin of the lower right sacral segments. Similar changes in the head, neck, and inter-trochanteric region of each femur.

the right clavicle with some cyst-like formation which might well represent metastatic neoplasm in bone. Similar but less extensive osteoclastic lesions were seen in the surgical neck and head of the left humerus.

Stereoscopic studies of the pelvis showed circular areas of bone destruction in each ischium and about the right acetabulum. There were suggestive changes in the iliac portion of the left acetabulum. The sacrum was not well visualized because of overlying gas shadows; however, there was a destructive process on the lateral margin of the lower sacral segments to the right. Similar changes were seen in the head, neck, and inter-trochanteric region of each femur.

Routine examination of the skull showed several rounded areas of translucency representing bone destruction in the parietal region bilaterally. A similar area was seen in the inferior portion of the parietal bone anteriorly just above the squamous

portion of the temporal bone. Another area was seen just anterior to the frontoparietal suture in its midportion on the right, and still another area was seen in the occiput on the left just inferior to the lambdoidal suture and near the midline. The internal auditory meatus on the right was larger than its fellow on the left, suggesting the possibility of neoplastic involvement. The sphenoid ridges and sella turcica were normal.

Examination of the spine showed a mild left dorsal scoliosis with no other evidence of abnormality. Antero-posterior projection of both forearms showed normal forearm, wrists, and metacarpals. The tibiae revealed no definite evidence of abnormality.

Course: During the first five days of hospitalization the patient's temperature varied between 100° F. and 103° F. Pressure, heat, and analgesics produced only temporary relief from pain in the right shoulder. On October 3, 1938 the patient was

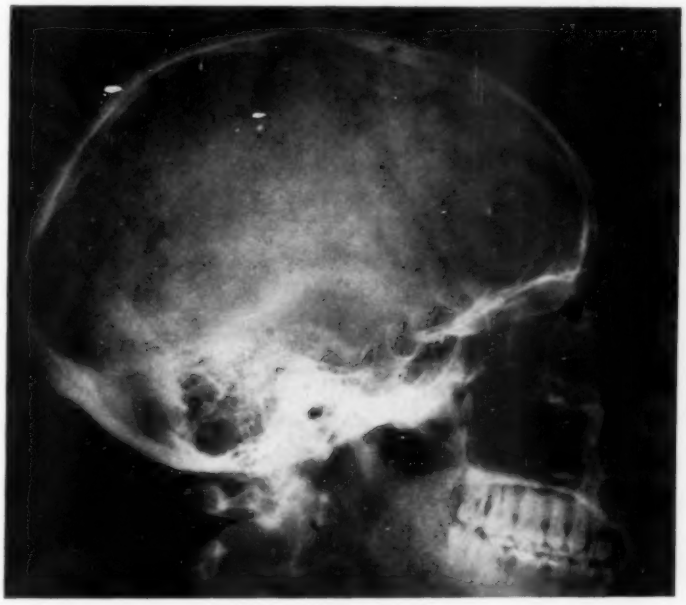

FIG. 3. Roentgenogram of skull, revealing several rounded areas of translucency representing bone destruction in the parietal region bilaterally. Similar areas seen in the inferior portion of the parietal bone anteriorly, anterior to the frontoparietal suture, and in the occiput just inferior to the lambdoidal suture.

given roentgen-ray therapy consisting of 400 roentgen units over an anterior right shoulder port. On the same evening the patient no longer felt pain or discomfort in the right shoulder and was able to sleep without sedation for the first time since admission to the hospital. On October 4, 1938, 400 roentgen units were given over the right shoulder posteriorly. That evening the patient voluntarily raised his right arm above his head and performed this action without pain. During the next four days the patient was given 400 roentgen units over each of four ports, two being anterior and two posterior. On October 9, 1938, the patient sat up in a chair for two hours. No further treatment was instituted, as it was felt that roentgen-ray therapy over splenic ports was contraindicated because of a white blood cell count of 26,100. On October 10, 1938 the patient became ambulatory, and was discharged on the morning of October 11, 1938. The hemoglobin maintained its level and on discharge was 59

per cent (9.1 grams per 100 c.c.) with a red blood cell count of 3,220,000 per cubic millimeter. At this time the patient experienced no pain or discomfort in the upper or lower extremities either on motion or at rest. The patient walked with a normal gait. He died January 1, 1939, at Michael Reese Hospital, Chicago, Illinois. No autopsy protocol was obtained.

Discussion

There is still some doubt as to the existence of the so-called monocytic cell type of leukemia, but there appears to be sufficient evidence (Wainwright and Duff,[24] Doan and Wiseman,[9, 17, 18 and 8]) to establish the identity of this particular disease.

The case, as far as can be ascertained, is the first in the literature in which there was an associated monocytic leukemia and bone absorption. The softening and absorption in the medullary portion of many of the long bones, the increased porosity produced by the widening of the Haversean canals, and the cystic changes which may be indicative of neoplastic invasion have been noted in cases of lymphocytic and myelogenous leukemia, but are new to monocytic leukemia as a clinical entity.

The relief which was given to the patient by roentgen-ray therapy over the painful extremities leads to the suggestion that roentgenographic studies should be undertaken in cases of monocytic leukemia with painful bony areas.

Conclusions

1. A case of monocytic leukemia with neoplastic bone involvement similar to that observed in other types of leukemia is presented.

2. Roentgen-ray therapy when applied over the affected bony sites appears to be beneficial in relieving pain.

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HYPERTENSION CAUSED BY UNILATERAL KIDNEY DISEASE*

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NUMEROUS reports of unilateral renal disease associated with hypertension have appeared in the literature since the epochal researches of Goldblatt. The purpose of this report is to add to the literature one more case of what seems to be a perfectly typical atrophic kidney which was associated with marked hypertension.

CASE REPORT

The patient, Miss M. J. M., aged 21, consulted one of us on May 3, 1941. She was referred by her family physician because of high blood pressure. Her family history was entirely negative. Her menstrual history likewise was perfectly normal. Her only illness during childhood was measles, except for some kidney trouble, the nature of which was not clear. She stated that she was in bed for several days but that there was no edema nor was there blood in the urine. She had had an occasional attack of tonsillitis. Her tonsils and adenoids had been removed in 1940. She also had had an operation for acute appendicitis at the age of 13.

Her complaint when first seen was that of headache. She stated that she had not felt well for the past six or seven months, having experienced fatigue and general malaise.

* Received for publication May 1, 1942.

Her headaches were basal in location and were present each morning on awaking. During the latter part of 1940 she developed an upper respiratory infection and at this time the physician who attended her took her blood pressure and found it to be 230 mm. Hg systolic and 120 mm. diastolic. From that time until I first saw her she

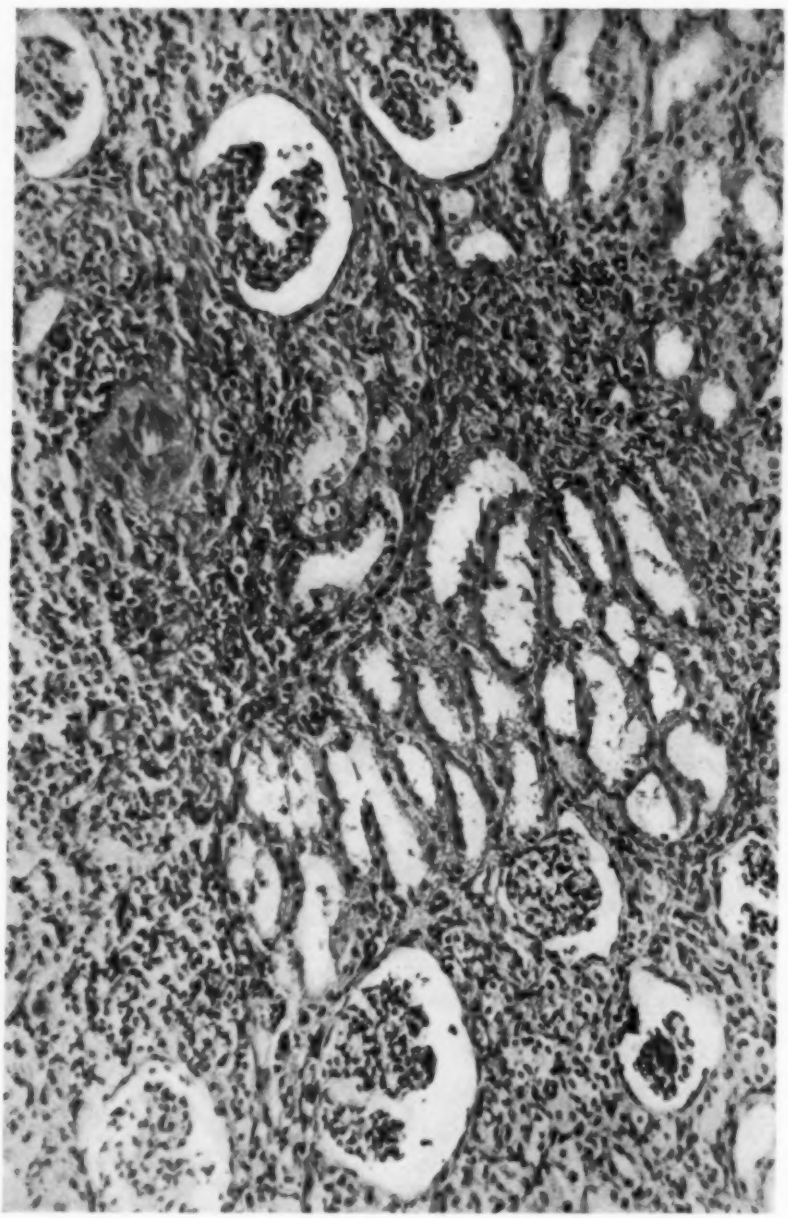

FIG. 1. Low power view of kidney cortex showing patchy condensation of parenchyma due to loss of glomeruli and tubules, and resulting scarring. Numerous small mononuclear inflammatory cells are seen in these frequent scar areas. The glomeruli and tubules in the intervening uninvolved areas show no significant changes.

had lost about 12 pounds, was quite nervous, and complained of considerable fatigue in addition to her headaches.

Physical examination revealed a rather thin, undernourished individual. There was considerable discoloration in the form of vasomotor reactions in her hands.

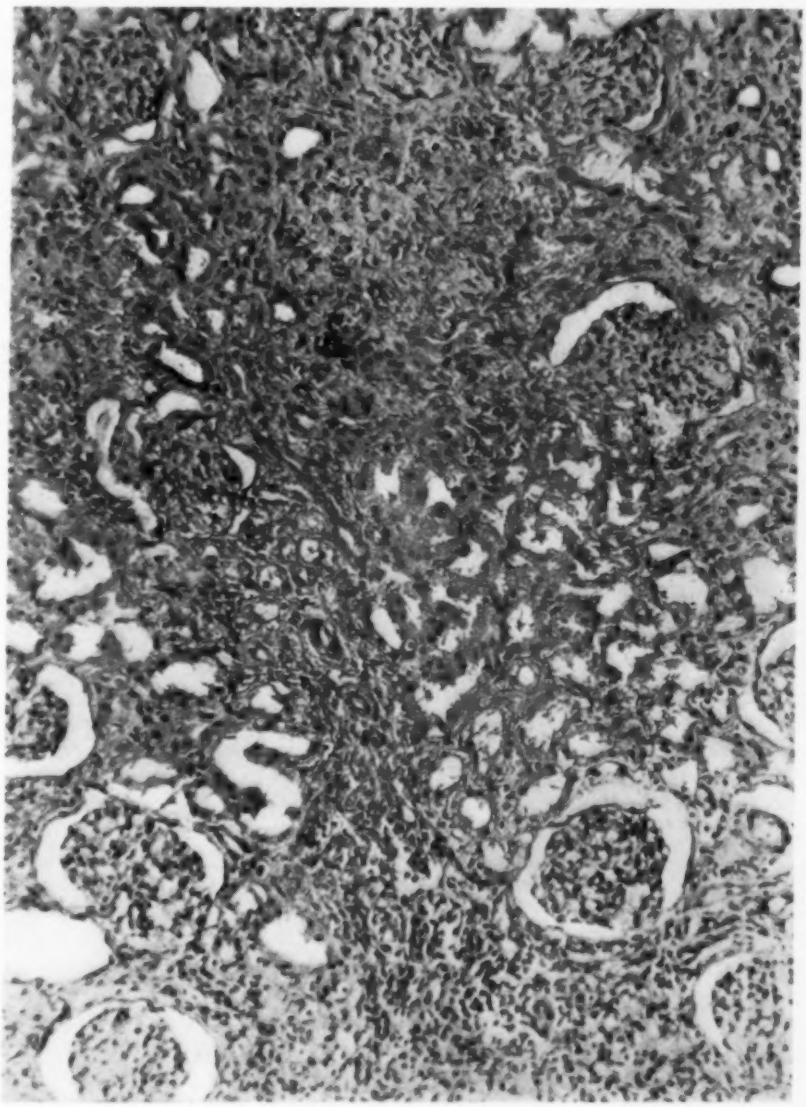

FIG. 2. In addition to the changes noted in figure 1, this low power view of kidney parenchyma shows thickening of the blood vessel walls with marked narrowing of the lumina.

There were some brownish pigmentations about her face, neck and forearms. Ophthalmoscopic examination revealed considerable tortuosity of the retinal vessels and there were areas where definite arterial spasm was noted. The vessels were moderately narrowed and there was some loss of light reflex. The discs were sharply

outlined. Ocular movements and fields of vision were normal. The pharynx was slightly congested. The teeth appeared more or less chalky. The submaxillary glands were palpable, as was the isthmus of the thyroid gland. There was some tenderness on fist percussion of the right kidney. Heart sounds were regular, distinct and quite forceful, with accentuation of the aortic second sound. The pulse rate was 100. The abdomen was scaphoid and negative except for a short McBurney scar. The left colon was palpable. There was no edema. Vibratory sense was normal. The hands were cold, discolored and moist. There was no tremor present. The pelvis was negative, as was the rectal examination. Blood pressure was 224 mm. Hg systolic and 154 mm. diastolic.

Lateral stereoroentgenogram of the skull revealed a normal sella turcica. There was a marked trace of albumin in the urine, a few hyalin casts, and an occasional red cell. Blood count was entirely normal. Blood urea nitrogen was 16 mg. per cent. Urea clearance was 127 per cent of normal. Phenolsulfonphthalein excretion was 82.4 per cent. Perirenal air studies were done and revealed nothing of consequence. A roentgen-ray film of the abdomen revealed a relatively small kidney on the right.

Dr. John M. Pace then investigated more thoroughly her urinary mechanism. Catheterized bladder urine was found to contain a small amount of albumin and granular casts. Cystoscopic examination was performed and indigo carmine was returned from the left ureteral orifice in a grade three concentration in 10 minutes whereas only a faint trace of blue was noted from the right ureteral orifice.

A retrograde pyelogram of the right side revealed a small kidney outline approximately one-half the size of the opposite kidney with a normal pelvis and calices. The left retrograde pyelogram was considered quite normal. Cystoscopy was repeated on the following day with the same findings as to the return of the indigo carmine. About 10 days later excretory urograms were made using Neo Iopax and good visualization was obtained of each kidney in five, 15 and 25 minute films.

About two weeks later the patient was subjected to another cystoscopy. Phenolsulfonphthalein was used intravenously and at the end of 45 minutes time 22 per cent of the dye was returned from the left kidney and none from the right.

This patient was observed for approximately two months, particular attention being paid to eye grounds and blood pressure. Her systolic pressure ranged from 210 to 240 mm. Hg and the diastolic level varied from 120 to 140 mm. Hg.

About the middle of June a definite fuzziness of the discs was noted. The patient at this time complained also of mild visual disturbance. She was advised that insofar as the right kidney was functionless, she had much to gain and nothing to lose by having it removed. She decided upon operation and on July 8 a nephrectomy was performed.

The removed kidney was approximately one-third its normal size. When the patient was returned to her room following operation, her blood pressure was 145 mm. Hg systolic and 85 mm. diastolic. Four hours later it was found to be 132 mm. Hg systolic and 100 mm. diastolic. The following morning her tension was 130 mm. systolic and 78 mm. diastolic. Twelve days later when she was discharged the reading was 126 mm. systolic and 78 mm. diastolic.

The kidney grossly was considerably smaller than normal. It measured 10 by 4 by 3 cm. and weighed 60.6 grams. The capsule was thickened but stripped readily and underneath there was a smooth shiny surface. On section the cortex and medulla were very well defined. The cortex averaged 4 mm. in thickness. There was no gross scarring in the parenchyma. The kidney pelvis was not enlarged. There were no stones.

Microscopically, sections through different portions of the kidney revealed very extensive focal chronic inflammatory changes immediately beneath the capsule (photo-

micrographs 1 and 2). In these areas was seen marked condensation of renal tissue with patchy scarring and with loss of tubules and glomeruli. A heavy small mononuclear cell infiltration occurred in these areas. Glomeruli in different states of degeneration were noted, whereas in striking contrast in the remainder of the renal parenchyma the glomeruli were essentially normal. The sectioned blood vessels were noticeably thickened, their lumina being reduced as much as one-third in diameter in numerous areas (photomicrograph 2). A section through the pelvis of the kidney revealed slight overgrowth of the pelvic mucosa. A few scattered chronic inflammatory cells were noted beneath. The pathologist, Dr. John L. Goforth, rendered the opinion that there was a chronic active progressive subcapsular pyelonephritis of marked degree.

The patient was seen on numerous occasions following her operation. Approximately two months following operation her eye grounds were strikingly different from the preoperative condition. The fuzziness had entirely disappeared about her discs, there was definite return of some light reflex and the spasm previously noted was absent.

Her blood pressure varied from 110 to 116 mm. Hg systolic with a diastolic of 72 to 78 mm. The patient gained 15 pounds and went back to her work. She was carefully checked in February 1942 at which time her blood urea nitrogen was 10 mg. per 100 c.c. and her urea clearance was 124 per cent of normal. Repeated urine examinations revealed nothing of consequence. Phenolsulfonphthalein excretion was 50 per cent in the first hour and 9 per cent in the second.

This patient presented only one interesting symptom following her operation, which was that of a momentary dizziness on arising from a recumbent position. This dizziness was rather marked a few months following operation but gradually became less severe, and when last seen the patient was entirely free of this annoyance. The only explanation one might offer for this interesting symptom is the obvious lack of cardiac and vascular adaptation to the changed levels of blood pressure. It is believed that this patient will continue a well individual; and she will be frequently observed for any possible disease in the remaining kidney.

Summary

A case of hypertension has been reported in detail which was apparently a result of unilateral kidney disease. The pathologic lesions of the kidney were comparable to those of the Goldblatt and Page experimental kidneys in hypertensive dogs.

For approximately one year the patient has been perfectly normal as far as blood pressure and general health are concerned.

Addendum: Since this case report was submitted, the patient has married and has given birth to a 7½ lb. baby with no difficulty. All during her pregnancy her blood pressure was watched carefully and the maximum reading was 122/82. Most of the readings varied from 106 to 110 systolic. Her kidney function remained quite normal throughout the period of gestation.

CHRONIC HYPERTROPHY OF THE SKIN AND LONG BONES: AN OSTEO-DERMOPATHIC SYNDROME*

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In 1926 M. Labbé and P. Renault [1] observed a case of "hypertrophic osteo-dermopathology." In 1927 Gronberg [2] described the syndrome "Magalia cutis et osseum." He collected nine similar cases from the literature in the preceding 16 years. In 1935, Touraine, Solente and Golé [3] designated and described "un syndrome osteo-dermapathique." This syndrome is characterized by lesions of thickened skin with furrowing of the scalp, forehead, face, and extremities associated with elephantiasis of the long bones without involvement of the joints. They reported several cases which had been previously classified as dermatological, associated with a pulmonary osteoarthropathy. These skin lesions were usually diagnosed as cutis verticis gyrata or pachyderma vorticella. Since these original reports Meilberger,[4] Roy,[5] Rintelen,[6] and Giomo [7] have reported cases of pachyderma with periostosis of the extremities, most of which, however, were associated with an elephantiasis of the eyelids.

Touraine et al. state that there are three clinical forms of their syndrome: the complete, the incomplete, and the incipient. In all these forms the skin lesion is pronounced (although there may be no scalp lesions in the incomplete form) and the bone lesions vary from extensive to slight changes and even complete absence. The characteristics of this syndrome are:

1. It affects young adults beginning before the twentieth year and is most apparent between 20 and 30.
2. It is limited to males.
3. It is not related to occupation. There is no familial history or history of syphilis.
4. The general health is not affected.
5. The skin becomes thick and furrowed especially over the forehead, face, scalp, hands and feet. No other parts of the body are affected.
6. There is a thickened periosteum which is bilateral and symmetrical.
7. The extremities show considerable hypertrophy due to thickening of the skin and periosteum.
8. The hands are enormous.
9. The nails are rounded like watch crystals.
10. There is normal mental state and no loss of libido.

Histological study of the involved tissue uniformly shows:

1. Enlarged excretory canals of the sebaceous glands.
2. An increase in the size and number of the sweat glands with tortuosity and lengthening of the excretory canals.

* Received for publication January 20, 1942.
From the Vascular Clinic, Department of Medicine, New York Post-Graduate Medical School and Hospital, Columbia University.

3. An increase in the size and number of elastic fibers in the corium.
4. The blood and lymph vessels may be normal but are more often enlarged.
5. There are frequently inflammatory infiltrations about the hair follicles, sebaceous glands, and blood vessels. These may sometimes form small areas of necrosis.
6. The subcutaneous fatty tissue is usually normal.

Case Report

A white male, aged 46, born in Italy, was admitted complaining of progressive difficulty in walking, and swelling of feet and legs, hands and forearms of nine years' duration.

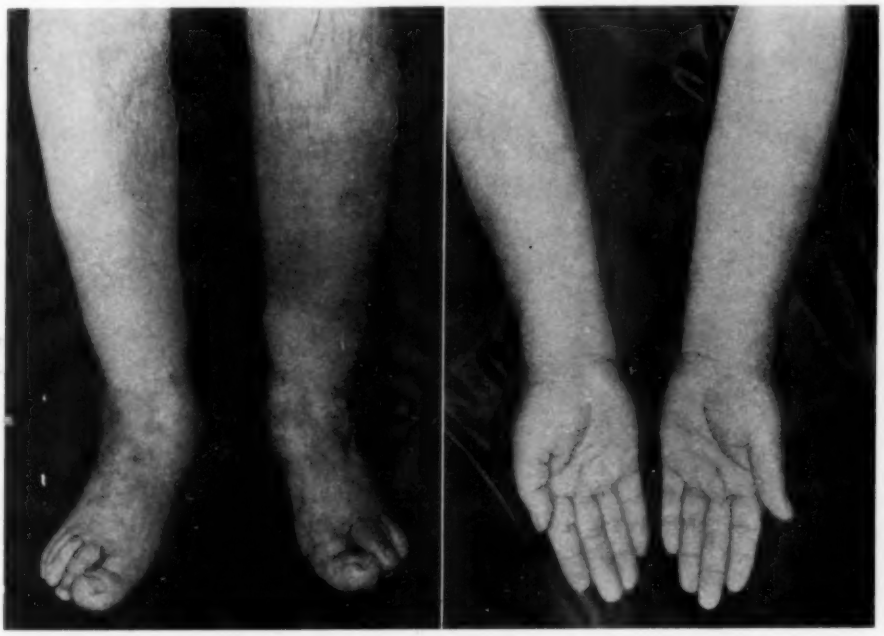

Fig. 1. (*Left*) Patient A.D. Hypertrophy of extremities due to thickening of skin and periosteum. Note sharp demarcation of joints.

Fig. 2. (*Right*) Patient A. D. Mild hypertrophy of hands and forearm without clubbing of fingers. Note accentuation of thenar folds.

Onset and Course: The present condition began about nine years prior to admission with pain in the left ankle. Then in chronological order the right wrist, left wrist, and the other ankle were involved. This was followed in a short time by swelling of the legs and then the forearms. There was no history referable to the vascular system such as claudication or rest pain except for an occasional twinge of pain in the knees. There was no history of phlebitis or varicose veins.

Past History: There had been no serious illnesses except for a fracture of the tibia and fibula of the left leg in 1922.

Family History: There was no history of any similar condition in any member of his family, past or present. There was no family history of vascular diseases, diabetes, syphilis, or tuberculosis.

Personal History: His occupation was that of a general building worker. He had been unemployed for several years. His habits were normal. He smoked cigars occasionally.

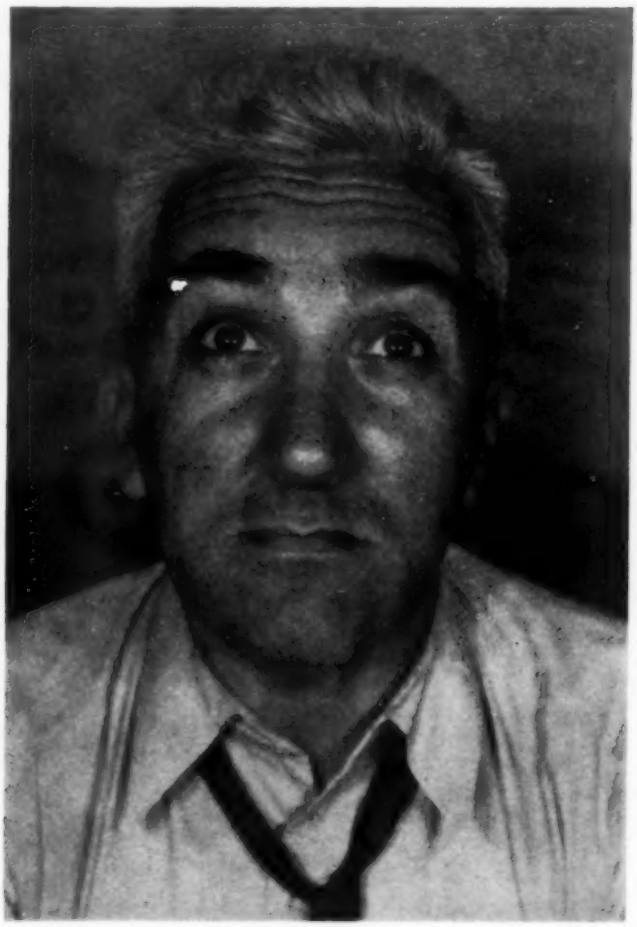

FIG. 3. Patient A. D. Thickening of skin over face with increased fold over forehead.

Review of Systems: All were negative except as noted in the chief complaint.

Physical Examination: This revealed a well developed, well nourished male about 45 years of age with thick coarse skin of light copper color. Mental reactions were slightly slowed. The nose, ears, and head were normal in size and proportion. There was no enlargement nor protrusion of the jaw.

Eyes: The pupils were equal and regular, reacting to light and accommodation. No abnormalities were noted in the fundi.

Nose and Ears: There was no obstruction nor discharge.

Chest: The chest was symmetrical and expansion was equal.

Heart: There were no murmurs. There was regular sinus rhythm. The point of maximum impulse was in the fifth interspace in the midclavicular line.

Lungs: Breath sounds and resonance were normal.

Abdomen: There was no rigidity, tenderness nor palpable mass. The liver, kidney and spleen were not palpable.

Scrotum: There was an edema of moderate degree.

Rectal: The prostate was small; the median sulcus was palpable. The epididymis on the left side was hard and indurated, but not tender.

Extremities: There was a marked brawny edema of the legs extending from the knees down to and including the feet, and of the forearms from the elbows down to and including the hands (figures 1 and 2). There was some pitting on deep pressure. The joints were only slightly involved in this swelling so that the lines marking the margins of the joints were greatly accentuated because of the surrounding edema. The skin was noticeably thickened in the extremities as well as over the face (figure 3). There were several small bluish discolorations on the legs. There was no clubbing of the fingertips nor of the toes.

This patient had been treated at another hospital in 1931 and again in 1937. The following diagnoses were received from this institution. *1931 Diagnosis:* Old fracture of the left tibia and fibula. Roentgenogram showed no evidence of fracture of bones of the foot. *1937 Diagnosis:* Retained roots; diseased tonsils; old healed fracture of the left tibia and fibula; infected ingrown toe nail; no evidence of thyroid disease. Laboratory: Basal metabolic rate plus 10; blood Wassermann reaction negative; blood chemistry normal; electrocardiogram showed left axis deviation.

Further laboratory studies were: Sedimentation rate (Westergren method) 54 mm. in one hour. Inorganic phosphate 2.3 mg. per cent (normal 3.5–4.0). Calcium 10.1 mg. per cent (normal 9.6–11.0). Phosphatase activity 4.8 units 2 hr. incubation (normal 3–5). Total serum protein 4.9 per cent; albumin 3.5 per cent; globulin 1.4 per cent; ratio 2.5.

Blood Wassermann negative on June 29, July 26 and August 17, 1939; Kline diagnostic test (July 24, 1939), negative. Kline exclusion test (July 24, 1939), plus-minus. Blood chlorides 480 mg. per cent (NaCl); blood cholesterol 185 mg. per cent; red blood cells 3,830,000, hemoglobin 12.35 gm. (74 per cent); white blood cells 8,800, color index 0.97. Differential: Polynuclear neutrophiles 65, polynuclear eosinophiles 3, monocytes 11, lymphocytes 21.

Repeated urinalyses were negative except for occasional white blood cells. Culture of the prostatic secretion on November 29, 1939, was positive for *Staphylococcus albus*. On November 22, 1939, test for hormones in the urine was strongly positive for Prolan.

Further blood chemistry determinations were:

	N.P.N.	Ca.	P.	Glucose	Protein	Phosphatase	Cholesterol
	in mg. per cent				per cent	units	mg. per cent
January 8, 1940.....	36.6	9.6	3.8	88.0	7.29 Alb. 4.32	3.58	
February 4, 1940.....		10.0	2.4		Glob. 2.97		
February 5, 1940.....		10.0				2.36	159.0 Esters 86.5

Physical Measurements:

	Legs and Arms			
	Right		Left	
	August 3, 1939	March 25, 1941	August 3, 1939	March 25, 1941
Above malleolus	11.0	10.5	11.75	12.0
4½ in. below patella	14.85	15.6	16.12	16.25
Lower margin patella	15.12	14.6	14.36	14.5
Upper margin patella	16.5	17.5	16.12	17.0
Above wrist	8.0	8.5	8.36	7.75
1 in. below antecubital fold	11.5	12.0	11.25	11.75
1 in. above antecubital fold	11.0	11.5	10.25	11.25

Weight on admission was 175 lbs., June 29, 1939. Weight at present, February 24, 1941, is 190.

Oscillometric readings:

	Right	Left
Foot	⅝	¾
Ankle	2.0	1¾

Course: This patient was followed in the Out Patient Department for a period of six months. During this period he was on a salt free diet. An attempt was made to reduce the edema by acetyl beta methyl choline chloride (mecholyl) therapy given by iontophoresis, and by physiotherapy. This was entirely ineffective. At the end of this period he was hospitalized for more complete study.

Because of the finding of urinary Prolan, androgenic therapy in the form of testosterone propionate was instituted and he was given 25 milligrams three times weekly. He received a total of 2025 milligrams over a period of 27 weeks. This was supplemented by the empirical use of nicotinic acid, thiamine chloride, and other factors of the B complex orally. Physiotherapy in the form of whirlpool baths and massage was also given.

In November 1940, almost one year after admission, the patient suddenly developed a temperature of 104° F., with a marked irregular reddening of the right arm. This completely subsided in 10 days with sulfanilamide therapy. Except for this incident, the patient's condition remained practically the same during the 21 months of observation. There was some softening of the brawny edema but no marked decrease in the size of the extremities. Roentgenographic studies at various intervals revealed no significant deviation from the original picture in the 13 months following admission. There was revealed some decrease in the amount of periostitis with moderate smoothening of the irregular margins. There was some recent rarefaction of bones of the hands and feet with formation of a cyst in the cuneiform bone. The skin did not appear to be as coarse or as thick. Altogether the changes were not remarkable. During the period of observation, laboratory tests remained consistently normal except for an elevated sedimentation rate.

Biopsy of Skin, Periosteum and Bone, December 11, 1939 (figures 4 and 5). *Microscopic:* Skin sections were covered with stratified squamous epithelium. The corium was much increased by thick fibers of hyaline fibrous tissue as in old scars. The elastic fibers were fragmented and appeared thinned near the surface, and thickened and knotted in the deeper layers. The sweat and especially the sebaceous glands were hypertrophied with parakeratosis in the ducts.

FIG. 4. Biopsy of skin from pretibial area of the right leg.

The bands of fibrous tissue union with the subcutaneous fascia were thickened. Here, the blood vessels had edematous walls with swelling and exfoliation of the intimal endothelium. At one point in the subcutaneous fascia there were several areas of calcific stippling.

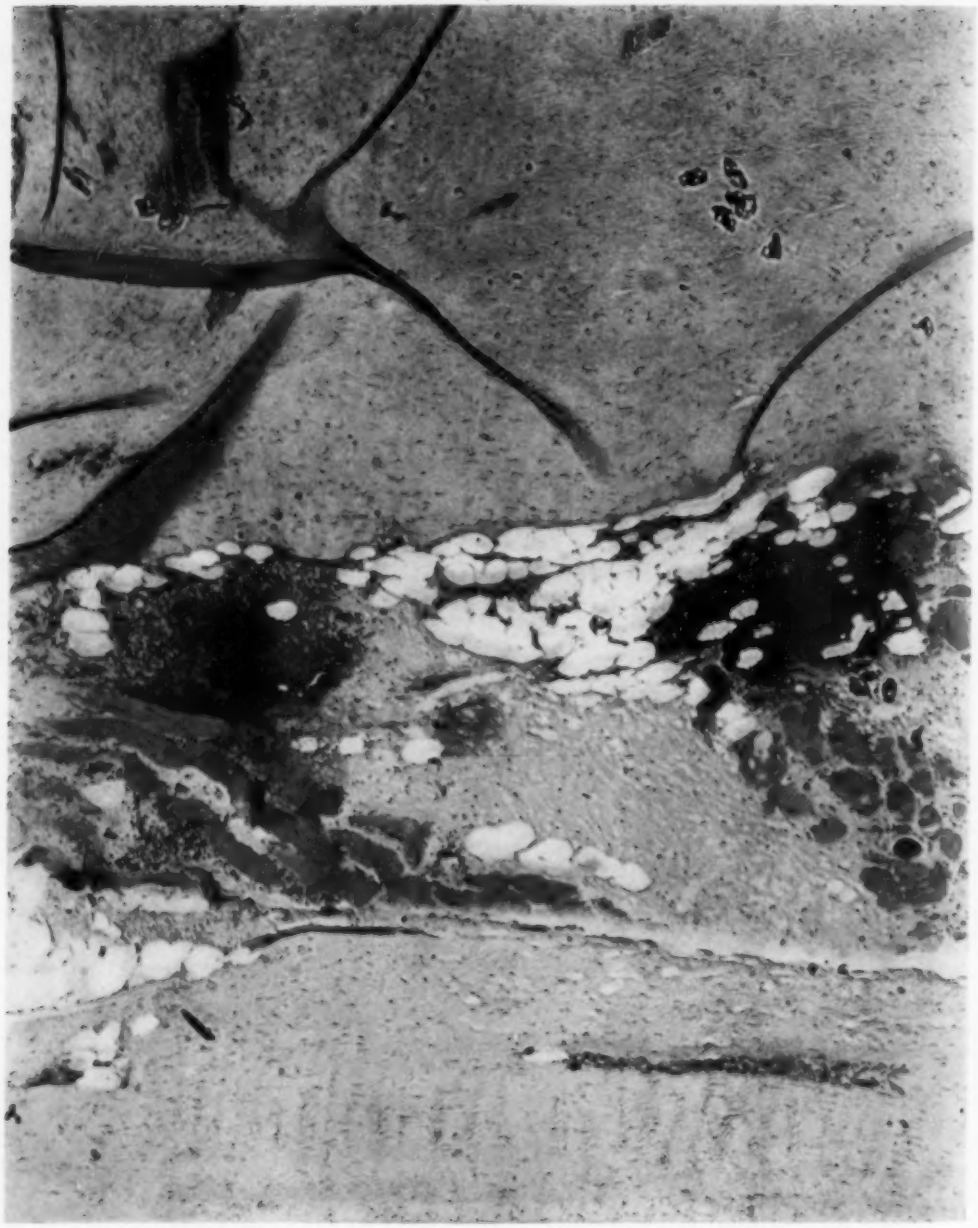

FIG. 5. Biopsy of right tibia.

The union of muscle bundles and fascia and periosteum was marked by proliferation of mesothelium and capillaries. Some vessels were surrounded by dense foci of lymphocytes and plasma cells and polynuclear leukocytes were occasionally seen in the vessel lumens. Lesser but similar changes were seen in the fascial strands extending through the fat from fascial layer to layer, and rarely between the muscle

fibers. The parperiosteal tissue showed the most elaborate foci formed chiefly of plasma cells, some of which were seen about the smallest capillaries. In these foci some cells were filled with old blood pigment.

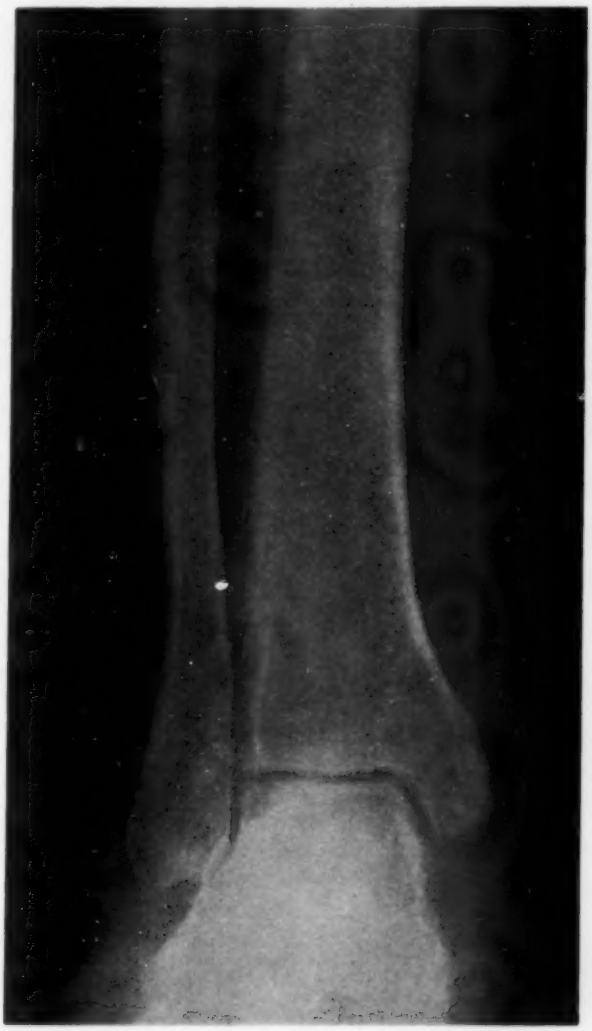

FIG. 6. Roentgenological study of right lower extremity. Note marked periosteal irregularity of both tibia and fibula.

The sections of decalcified bone showed a porositic cortex with the marrow spaces enlarged. The periosteal surface suggested some slight previous activity, i.e., young periosteal cells but no osteoclasts, now quiescent.

Diagnosis: Chronic productive dermatitis with hyperplasia of glands. Chronic productive inflammation of parperiosteal tissues, parosteitis. Osteoporosis.

Differential Diagnosis: Due to the predominance of the periosteal lesion and bone changes in this case several other conditions must be considered.

Hypertrophic Pulmonary Osteo-arthropathy. This was first described as an "ossifying periostitis" in 1889 by Bamberger.[8] This was closely followed in 1890 by Pierre Marie,[9] who described a series of cases called "osteoarthrompthie hypertrophiante pneumique." Since that time some 150 cases have been reported in the literature, less than 10 per cent of which were without a primary disease such as pulmonary tuberculosis, congenital heart disease, etc.[10] In this disease one usually finds: (1) The presence or history of some respiratory or heart disease. (2) Usually no enlargement of the soft parts of the extremities except for clubbing or bulbous swelling of the tips of the fingers and toes. (3) Symmetrical deposits of new subperiosteal bone. (4) Sometimes sclerosis and thickening of the cortex. (5) Curving of the nails in all directions. (6) Atrophy of the cancellous tufts and elongation of the terminal phalanges, often with hairlike calcareous strands projecting toward the nail.

Familial Acromegalic-Like Skeletal Disease. Previous to and following the work of Bamberger and Marie, Arnold,[11] and later Oehme [12] and Muller,[13] and more recently Freund [14] described a condition which they called idiopathic familial generalized osteo-phytosis or familial acromegalic-like skeletal disease.

The differential characteristics are: (1) Onset of the disease at puberty. (2) Progression by exacerbation. (3) Extreme degree of bony change. (4) Tendency of the syndrome to be familial. (5) Very little if any thickening of the soft tissues. (6) Clubbing of the finger tips.

Acromegaly. This may be differentiated by its characteristics: (1) Enlargement of the sella turcica. (2) Changes in the calvarium such as thickening, etc. (3) Prognathism. (4) Polyphagia with an increased basal metabolic rate. (5) Overdevelopment of the cancellous tufts and adjacent soft tissues of the terminal phalanges. (6) Elongation of the phalanges.

Osteitis Deformans. This may be differentiated since in this disease there is: (1) No enlargement of the soft parts. (2) Tendency to curving of the tibia and other long bones. (3) Tendency to asymmetrical enlargement. (4) Tendency of the coarse striae to cross each other at sharp angles with broad coarse spaces between the striae, demonstrated by roentgenographic examination of the bones. (5) Thicker and less dense cortex than is normally seen.

Chronic Venous Stasis. This may produce proliferation of the bone so that one may find the same changes in the distal portions of the extremities as noted in some of the aforementioned conditions. Changes in the blood supply have a definite effect on bone growth in that increase in length and breadth of an entire bone is possible, as is sometimes seen with an arteriovenous anastomosis. Proliferation of a portion of a bone is also possible as for example with small lymphangiomata. However, in this case there were no varicose veins or other evident defects in the venous system and there were definite changes in the skin of the face.

Syphilis. Syphilis of the bones is so similar that it must be ruled out by the absence of associated findings. It may be differentiated since: (1) A syphilitic periostitis most often assumes a lace like pattern which is not to be confused with this pachyperiostosis. (2) There is a positive Wassermann reaction in about 70 per cent. (3) There are skin, cardiovascular, or central nervous system findings present. (4) There is usually a history of a primary lesion.

Repeated blood Wassermann, Kline and Kahn tests including a provocative Wassermann were consistently negative in our case. There were no associated findings to suggest a syphilitic infection.

Discussion

This patient presents a definite pachyderma which is not characteristic of that found in chronic lymphedema or in cutis verticis gyrata. Clinically the normal lines of cleavage of the skin are only slightly accentuated. Microscopic examination, however, reveals an almost identical picture with the characteristic parakeratosis and focal areas of inflammation as described by Touraine, Solente, and Golé. There is in addition a pachyperiostosis and osteophytosis. There were no biopsies of periosteum or bone performed in the cases previously reported. Our cases cannot, therefore, be compared histologically with them. There is a definite similarity in the bones affected. There is agreement as to the age, sex and general health. The onset and progression were insidious, so that the patient did not particularly notice any change from normal until the joint symptoms appeared.

This case, however, presents several differences. The age of onset was approximately 35 which is somewhat older than that of the reported cases. The finger nails are normal in contour. One of the cardinal features, as described originally by Touraine, Solente, and Golé, is the marked furrowing of the skin. In the three clinical types described, the dominant feature is the skin lesion with variations in the periosteal lesion even to complete absence. The dominant feature in our case is the periosteal lesion with the skin furrowing a less prominent sign.

There is no evident etiological factor of the disease in this patient. One has to consider dysfunction of the endocrine system as a possible cause. The presence of Prolan in the urine might indicate an excessive production of estrogens. What possible effect excessive estrogens in the male have on the calcium metabolism is still a research problem.

In 1938 Gardner and Pfeiffer,[15] and in 1940 Sutro,[16] reported that in the mouse, injections of estradiol benzoate over a long period of time produced marked disturbances in calcium. The pelves showed resorption and the long bones showed an increase in density due to replacement of the bone marrow by bone spicules. Later, Wentworth, Smith and Gardner [17] reported that the continued use of large doses of estradiol benzoate in mice produced in addition, significantly higher concentrations of inorganic substances in the femurs and pelves than in control mice, or mice receiving testosterone propionate, or estradiol benzoate plus testosterone propionate.

In our case the bone marrow was not involved as far as roentgenographic studies could determine. There was, however, evidence of resorption in part of the skeletal structure and excessive calcification in others.

It is interesting to note that where these bone changes were produced experimentally with estradiol benzoate, a regression could not be secured with testosterone propionate therapy. Androgenic therapy was ineffective in our patient.

Infection may also play a rôle in the production of this syndrome. Our patient had evidence of chronic infection in the teeth and prostate. (Eight abscessed teeth were removed during this observation period.) The increased sedimentation rate may be an indication of such a process or may be due to the process itself. The sudden occurrence of a spontaneous lymphangitis in the right arm would point to the possibility of a chronic streptococcus infection.

Conclusion

1. A case of pachydermatitis with pachyperiostosis of the extremities (Touraine-Dolente-Golé syndrome) is presented with a differential diagnosis.

2. The presence of an excessive amount of estrogens in the male is suggested as a possible etiological factor of the syndrome in this patient.

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SPONTANEOUS ARTERIOVENOUS COMMUNICATION BETWEEN THE AORTA AND SUPERIOR VENA CAVA *

By LAMONT R. SCHWEIGER, M.D., HOWARD B. BURCHELL, M.D., and ARCHIE H. BAGGENSTOSS, M.D., *Rochester, Minnesota*

SPONTANEOUS communications between the large arteries and veins of the thorax occur with sufficient rarity to warrant a report of the following case.

CASE REPORT

A white woman, aged 45 years, registered at the Mayo Clinic December 16, 1940. She apparently had been well until two years before her registration at the clinic. At that time she had noted that she became fatigued very easily. Approximately one year before she came to the clinic she had noted that dyspnea and palpitation occurred on exertion. Because of the increasing severity of these symptoms in the next six months, she had been forced to curtail her activities and to remain in her home. For six weeks before she came to the clinic her face, neck and anterior and posterior walls of the thorax had been swollen. The face was said to have been more swollen on the left side at the onset, but soon thereafter the right side became more markedly involved. There had been no orthopnea, paroxysmal dyspnea, thoracic pain or peripheral edema. One week after the onset of swelling, a mild infection of the upper part of the respiratory tract had occurred. This infection had aggravated the dyspnea. Two weeks before her arrival at the clinic, the patient had noticed prominent veins in the anterior wall of the thorax. The clinical history disclosed no other significant data.

The significant observations on physical examination were as follows: There was moderate cyanosis of the face, ears and fingers. The face, neck, and thoracic walls were moderately edematous, but there was little swelling of the arms. Numerous dilated superficial veins were observed over the anterior thoracic wall. There was no swelling of the lower extremities. The maximal cardiac impulse was at the midclavicular line, and the heart rate was 100 per minute and regular. The blood pressure was 150 mm. of mercury systolic and 38 mm. diastolic. A continuous loud murmur with systolic accentuation was present over the upper part of the sternum and was heard with greatest intensity at the aortic area. A soft diastolic murmur, seemingly distinct from the first murmur, was heard at the left sternal border. In addition, a continuous thrill with systolic accentuation was palpable over the same area. Pistol-shot sounds were present over the femoral arteries and the peripheral pulse was collapsing in character.

Examination of the eyes revealed normal reflexes and essentially normal visual fields. The fundi exhibited marked fullness of the retinal veins which pulsated strikingly, and there was a definite synchronous pulsation of the retinal arteries. This simultaneous pulsation of both arteries and veins was the striking feature of the funduscopic examination.

A diagnosis of a communication between the ascending aorta and the superior vena cava was made.

The relevant laboratory findings were as follows. The urine, except for albuminuria, grade 2, was normal. The concentration of hemoglobin was 10.6 gm. per 100 c.c. of blood. The erythrocyte and leukocyte counts were 4,240,000 and 5,000 respectively, per cubic millimeter of blood. The following results were obtained with serologic tests for syphilis. The Kline test was 4 plus; Kahn's test was 3 plus; the

* Received for publication December 15, 1941.

Hinton test was positive; and Kolmer's test was very strongly positive. Roentgenologic examination of the thorax revealed dilatation of the supracardiac shadow (figure 1) and enlargement of the cardiac shadow to the left. Roentgenoscopic examination of the thorax revealed a diffuse aneurysmal dilatation of the ascending aorta associated with a diffuse widening of the supracardiac shadow. The electro-

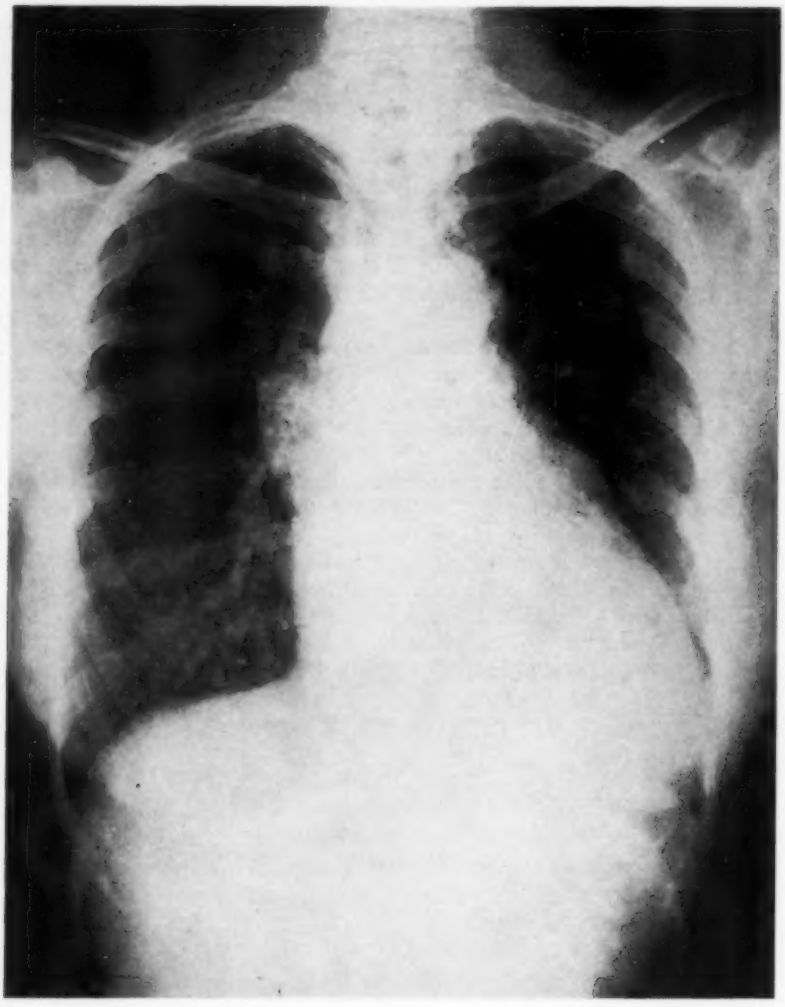

FIG. 1. Increase in width of supracardiac shadow, and cardiac enlargement.

cardiogram was not noteworthy except for right axis deviation (figure 2). The venous pressure, estimated directly, was 52 cm. of water in the right arm and 51 cm. of water in the left arm. There was no distention of the veins of the legs and the venous pressure was not measured in them. The oxygen content, oxygen capacity and oxygen saturation of the arterial and venous blood are shown in table 1.

An attempt was made to demonstrate the collateral circulation and the communication between the aorta and the superior vena cava by injecting 10 c.c. of a

sterile solution (35 per cent, weight/volume) of diodrast (3, 5-diiodo-4-pyridone-N-acetic acid and diethanolamine) into an antecubital vein of each arm simultaneously. This attempt was unsuccessful as only a few collateral channels about the shoulders were visualized.

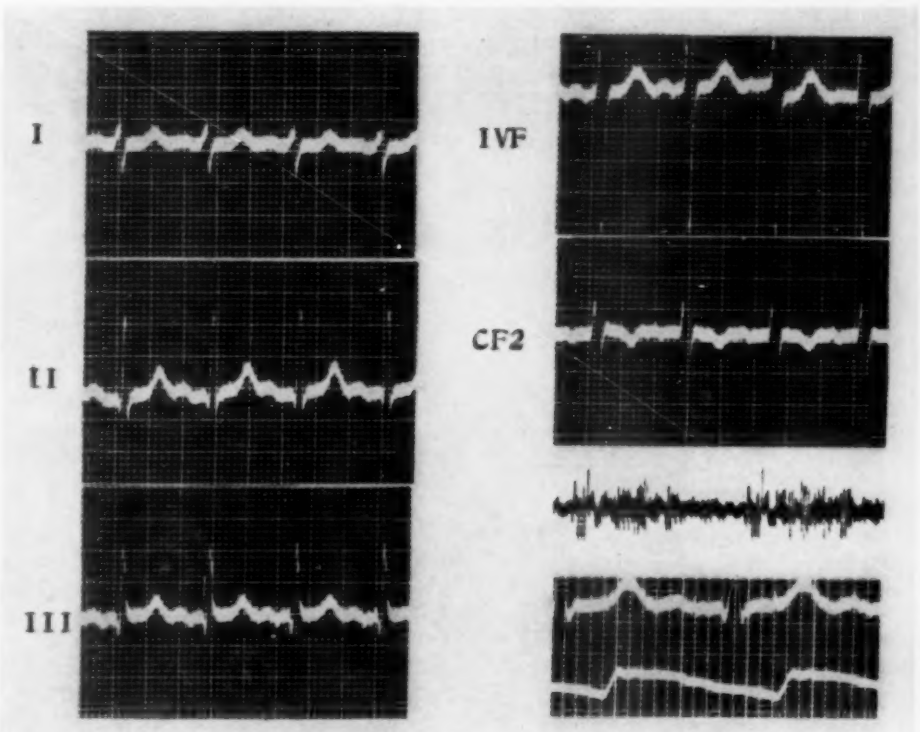

FIG. 2. Electrocardiogram and sound tracing demonstrating moderate right axis deviation and the associated inversion of the T-wave in the CF_2 lead. The recorded murmur is seen to be continuous with systolic accentuation.

During the few weeks following the patient's dismissal from the clinic, there were increasing symptoms and signs of congestive heart failure which terminated in the patient's death approximately one month after leaving the clinic.

Dr. D. O. Manhardt, who performed the necropsy at our request, removed the heart and great vessels en masse and sent them to us for examination. The heart weighed 365 gm. There was a slight amount of fibrinous exudate over the

TABLE I

Oxygen Content, Oxygen Capacity and Oxygen Saturation of Arterial and Venous Blood

Source of Blood	Oxygen Content, c.c. per 100 c.c. of Blood	Oxygen Capacity, c.c. per 100 c.c. of Blood	Oxygen Saturation, Per Cent
Vein of arm	2.68	14.39	18.6
Vein of leg	7.26	14.06	51.6
Femoral artery	12.42	13.86	89.6

right ventricle. The ascending and transverse portions of the aorta were dilated, and a sacculated aneurysm, which measured 8 cm. in its greatest diameter, had originated from the ascending portion. The aneurysm protruded superiorly, posteriorly and to the right (figure 3). The intimal surface was wrinkled and contained longitudinal striations, numerous whitish elevations and some atheromatous plaques. The orifices of the coronary arteries were not appreciably compromised. The portion of the aorta which made up the aneurysm also had the wrinkled appearance associated

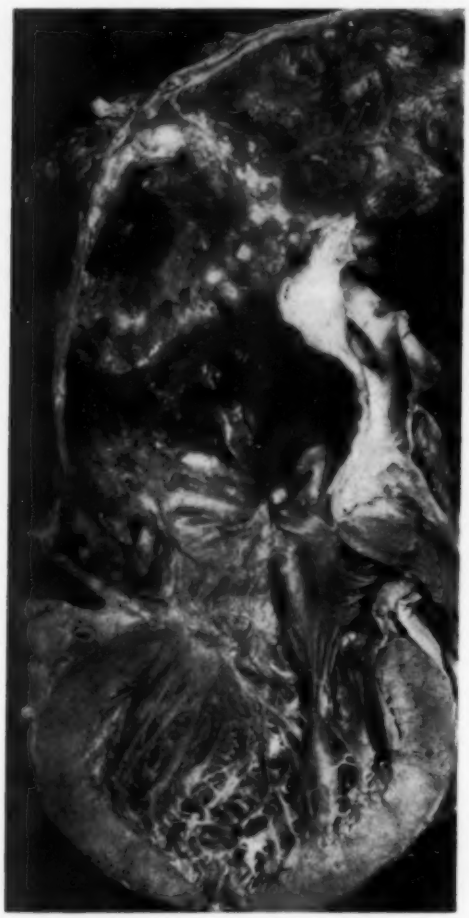

FIG. 3. Aneurysm of the ascending aorta associated with saccular protrusions, dilatation of the aortic ring, and cardiac dilatation and hypertrophy.

with syphilitic aortitis. In the posterolateral aspect of the sac, where the greatest thinning had occurred, there were two openings which communicated with the superior vena cava. The larger opening was roughly oval in shape, had a ragged edge and was 5 mm. in its long diameter. It was situated about 7 cm. above the aortic valve. Immediately below this opening was a smaller one which was 2 mm. in diameter.

The superior vena cava was not remarkable except for a moderate degree of dilatation and the presence of a small, flat, mural thrombus in the region of the arteriovenous fistula. Aside from the dilatation and moderate hypertrophy, the heart

was not remarkable except for the appearance of the aortic valve. The cusps were shortened and the edges had a thickened, rolled appearance. The cusps were slightly thickened and there was some separation at the commissures between the right and posterior cusps. The circumference of the aortic ring was 8.5 cm., that of the mitral orifice was 8 cm., that of the tricuspid valve 12 cm. and that of the pulmonic valve ring was 7.5 cm. The left ventricle was 7.5 cm. in depth and the thickness of its wall was 1.5 cm. The right ventricle was 9 cm. in depth and varied between 3 mm. and 7 mm. in thickness. The coronary arteries were freely patent throughout their course although there were a few intimal plaques.

In sections of the ascending and transverse portions of the aorta the most significant abnormalities were the presence of collections of lymphocytes in the media and adventitia, marked destruction of the elastic laminae and scarring by hyaline connective tissue. In the intima there were marked scarring, folding and indentations corresponding to the longitudinal scars noted grossly. There were also a few patches of atherosclerosis and calcification. In the region of the fistulas, the adventitia of the ascending aorta was firmly fused with the wall of the superior vena cava. At the borders of the fistulas, there were patches of necrosis and fibroblastic proliferation. In this region, the aortic wall had become greatly thinned and much of the muscular and elastic tissue had been replaced by hyalinized connective tissue.

In the wall of the superior vena cava there also were collections of lymphocytes, destruction of elastic tissue, and an increase in the amount of fibrous connective tissue. Sections through the edges of the perforations revealed necrosis of the walls and an attached layer of fibrin.

Sections of the descending, thoracic and abdominal portions of the aorta revealed similar but much less striking changes than those in the ascending and transverse portions. Sections of the aortic valve revealed that the cusp had been greatly thickened at the free margin by fibrous connective tissue. Focal regions of fibrosis were found in the myocardium.

The following anatomic diagnoses were made: (1) syphilitic aortitis and aneurysm, (2) arteriovenous fistula (aorta to superior vena cava), (3) chronic syphilitic aortic valvulitis and insufficiency, and (4) hypertrophy of heart (365 gm., calculated normal weight, 288 gm.).

Comment

In an analysis of the reported cases of spontaneous communications between the large arteries and veins of the thorax, Armstrong, Coggin and Hendrickson were able to collect 124 cases of this condition up to 1938. Furthermore, these authors said that in more than 19,000 postmortem examinations at the Los Angeles County Hospital, only two cases of this condition had been seen. In the postmortem records of the Mayo Clinic this is the only instance of the condition that has been encountered.

Armstrong, Coggin and Hendrickson, in their analysis of the reported cases, noted that although the incidence of thoracic arteriovenous aneurysm attributed to syphilis was less than 50 per cent, this figure was undoubtedly too low. In support of this premise, they called attention to the fact that 26 cases have been collected since 1925 and in 20 of these cases there was definite evidence of syphilis. Moreover, in two of the 26 cases necropsy had not been performed and the clinical records were unavailable in one case. Thus, excluding these three cases, there was positive evidence of syphilis in 87 per cent of the cases.

The characteristic signs of an arteriovenous communication were present in the case which we have reported. During the 10-day period the patient was

under our observation, the pulse rate was consistently elevated, the pulse pressure remained high, and the characteristic continuous murmur and thrill, with systolic accentuation, were noted. The venous pressure in the legs apparently was not elevated and this is in agreement with other observations of a normal venous pressure in that part of the circulation not directly involved in the abnormal communication. The marked elevation of the venous pressure in the upper extremities was interpreted to be due to the passage of blood, under arterial pressure, into the vena cava although partial obstruction of the superior vena cava by pressure of the contiguous aneurysm may have played a part. The failure of diodrast, injected simultaneously into both antecubital veins, to be demonstrable in the superior vena cava on roentgenoscopic examination is taken as further evidence for this conclusion. The pronounced oxygen desaturation of the venous blood in the upper extremities when compared with that for the lower extremities was again an important finding that was consistent with the lesion.

In the postmortem findings it is to be noted that the heart was dilated but not greatly hypertrophied, as judged by its weight. The absence of prominent cardiac hypertrophy together with right axis deviation in the electrocardiogram gives us some reason to believe that the terminal cardiac failure and dilatation might have been due mainly to the arteriovenous communication. The onset of swelling of the face, neck, and walls of the thorax approximately six weeks before the patient appeared at the clinic, and the fact that the patient died one month after her dismissal from the clinic, probably indicate that the communication between the aorta and superior vena cava had been present for approximately three months. We should like to emphasize the long survival time after the development of the communications between the aorta and the superior vena cava.

Summary

In the case of abnormal communication between the aorta and superior vena cava that we have just reported the characteristic signs of an arteriovenous fistula in the thorax were present. Attention is directed to the relatively long duration of life after the establishment of the communication.

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EDITORIAL

THE WAR AND MEDICAL EDUCATION. II

ONE year ago this column [1] was devoted to a discussion of the various problems in medical education that had arisen as a result of the war. At that time, the majority of medical schools in this country had already adopted an accelerated program with the admission of a new class every nine months and continuous instruction the year around, thus making it possible for the medical student to obtain the degree of Doctor of Medicine in three calendar years.

As potential disadvantages of this accelerated program, it was pointed out that the students—not to mention the depleted and overworked faculties—might grow stale under the pressure of such an intensified schedule and that many of the students might find the increased financial burden a difficult hurdle to surmount. Undoubtedly all medical students have felt the strain of uninterrupted concentrated study; a few are frank to admit that they have "grown stale" and are not deriving full benefit from their courses. Moreover, neither the decrease in weight nor the increase in furrows among the professors and instructors can be attributed solely to food-rationing. But on the whole, the accelerated program has worked out very well to date and more than justified its adoption in the number of new medical officers that are soon to be rendered available for active duty with the armed forces. The financial problem has been completely eliminated for the majority of medical students since the inauguration of the Army and Navy training programs.

Late in 1942, the draft age limit was lowered to 18 years. It was obvious that new legislation would be necessary to insure an adequate supply of qualified premedical students to fill the classes entering the medical schools every nine months. The answer to this problem was soon to come with the creation of the Army Specialized Training Program (A.S.T.P.) and the Navy College Training Program (V–12). These programs permitted medical and premedical students to enlist in the reserve corps of the army or navy and to carry on their studies while under the jurisdiction of military officials.

For the time being, training in medicine under the A.S.T.P. is limited to enlisted men currently in attendance at approved medical schools and enlisted men who have been accepted for future entering classes by medical schools that are participating in the A.S.T.P. In other words, any enlisted man in the army who has passed the qualifying tests for the A.S.T.P. may apply for admission to the medical school of his choice anywhere in the country and, if accepted, he will be assigned to an A.S.T.P. college unit to complete his premedical training at the government's expense before entering medical school. Civilian students who have completed their premedical

[1] The war and medical education, Editorial, ANN. INT. MED., 1942, xvii, 874–876.

training under a 2–A selective service classification and have been accepted by an approved medical school may apply to their draft boards for voluntary induction with the request that they be assigned to the A.S.T.P. unit at that medical school. The army has honored such requests for assignment to classes entering affiliated medical schools in 1943 and 1944.

At the present writing, the Navy V–12 Program for *premedical* students is further advanced than the Army Specialized Training Program. The Navy has established V–12 units for premedical training at several colleges in each naval district. A student in such a V–12 unit who was admitted to an affiliated medical school prior to July 1, 1943 will be permitted to attend that medical school, provided he has been admitted to the first entering class for which he is eligible after the completion of his premedical course. All other V–12 premedical students must apply for admission to medical school through the commanding officer of their unit. They are allowed to specify their first, second, and third choice medical schools on their application, but the majority will probably be assigned to medical schools with V–12 units located in the same naval district. A board of deans has been set up in each naval district to assist the Navy in selecting from the V–12 college units students who seem qualified for the study of medicine and in assigning these students to medical schools. It seems likely that the Army will set up a similar system for assigning premedical students in the A.S.T.P. to classes enrolling in medical schools in 1945.

So much for the army and navy programs as they apply to premedical students. Early last summer the majority of *medical students* who were physically acceptable for military service enlisted in either the A.S.T.P. or the Navy V–12 program. Those students who already held reserve commissions (on an inactive status) of second lieutenant in the Medical Administrative Corps of the Army or ensign (HVP) in the Navy were granted the option of resigning their commissions in order to join the Enlisted Reserve of their respective services. All enlistees were formally inducted into the army or navy, issued uniforms, and designated cadets with the pay and maintenance allowance of a private in the army or an apprentice seaman in the navy. The army cadets wear the uniform of a private whereas the navy cadets are attired in uniforms similar to those worn by the midshipmen at Annapolis. The students in both enlisted reserve corps are subject to military discipline with a certain number of hours of military training and instruction every week, but it is commendable that in general the military authorities have made every effort to interfere as little as possible with the medical curriculum. The scientific instruction and administration of the medical schools is left entirely in the hands of the faculty and administrative officials of the schools who retain full power to drop a student for academic failures. If a cadet fails any of his courses, the failure must be reported to his commanding officer who in turn may at his discretion recommend that the cadet be separated from his medical unit and assigned to some other

branch of the service. Furthermore, the commanding officer may at any time separate a cadet from his unit for "behavior unbecoming to an officer." The Army and Navy have contracted with the medical schools to defray the tuition of the cadets and to furnish the cadets with most of the technical equipment and textbooks that they require for their medical course. On the other hand, those students who elected to keep their reserve commissions (2nd Lieutenant in the Medical Administrative Corps or Ensign HVP) remain on an inactive status in civilian attire and must defray all the expenses of medical school and maintenance out of their own pockets. The financial advantage to the students of resigning these commissions and joining the enlisted reserve is obvious.

The internship-residency system has always occupied a most important place in basic postgraduate education of newly graduated physicians. The hospitals of the United States with the approval of Procurement and Assignment Service have recently adopted the nine-nine-nine month plan [2] for the allocation of interns and residents in 1944. This plan involves three major changes: (1) internships and residencies are being changed over from a twelve to a nine month base period to remedy the difficulties inherent in a nine month medical school year and a twelve month hospital year; (2) certain essential commissioned men will be permitted to give some service as hospital residents instead of being ordered to active duty immediately upon the completion of their internships; (3) interns as well as residents are included in the allocation plan. This proposal has been conditionally accepted by the Surgeons General of the Army and Navy in the following form: (1) the internship shall be reduced to nine months; (2) one third of the interns who hold commissions in the Army and Navy may be deferred for nine months (tenth to eighteenth months) as assistant residents; (3) one-half of this number or one-sixth of the total number of commissioned interns may be deferred for an additional nine months (nineteenth to twenty-seventh months) as residents. Under this plan, two-thirds of all commissioned interns now in hospitals will be eligible for orders to active duty on or about January 1, 1944 and at about the time the new graduates will begin their internships. The Procurement and Assignment Service believes that minimum adequate hospital medical service can be provided only if each hospital exerts every effort to obtain and retain women and physically disqualified house officers, since the number of men to be deferred by the armed services will not be adequate to meet even the minimal needs for hospital residents. The overall cut will be about one-third. For the average hospital the allocation for 1944 will be somewhat less than two-thirds of the 1940 number of residents and two-thirds to three-fourths the 1940 number of interns. Such a curtailment of hospital staffs is bound to lower the quality of service that the hospital will be able to render patients as well as to deprive the house officers themselves

[2] Plan for the allocation of interns and residents in hospitals, 1944, Jr. Am. Med. Assoc., 1943, cxxiii, 98.

of the more thorough training that was available to them in the past. However, it seems to be the best solution that can be offered under current wartime conditions, and it is to be hoped that these young men will be afforded the opportunity for further service in hospitals during the post-war period.

Lastly, an extensive program for postgraduate medical instruction, especially designed for medical officers on active duty at the present time, has been developed by the Central Committee of the Wartime Graduate Medical Meetings. The national consultants have compiled the names of prominent men throughout the entire country who will serve on a national faculty. This faculty will assist the regional committees in meeting the demands for teachers. The American College of Physicians may take just pride in the fact that it anticipated the need for just such postgraduate instruction and indeed organized a number of such regional meetings early in 1943.

It is gratifying to record that our system of medical education has proved sufficiently flexible to meet the various exigencies occasioned by the war and to adjust itself so smoothly to the radical changes which we have briefly outlined.

W. H. B.

REVIEWS

Neurology. By Roy R. Grinker, M.D. Third Edition. 1136 pages; 26 × 17 cm. Charles C. Thomas, Springfield, Illinois. 1943. Price, $6.50.

This third revision of an already familiar and accepted textbook evidences a complete re-reading and appraisal not only of fact but of the manner in which it is presented. In both respects, welcome changes have been made.

In previous editions the chapters covering the anatomy and physiology of the nervous system were largely separate from those dealing with clinical data. Insofar as is possible, these fundamental data have now been incorporated with the clinical material. This regrouping has been of great help.

Much has been added, particularly concerning the chemistry of the brain. The discussion of epilepsy has been amplified through the inclusion of electroencephalographic data. A delightful chapter on cerebral neoplasms, contributed by Paul C. Bucy, entirely replaces the previous treatment of this subject.

Re-writing of much text with deletion of occasional needless words or phrases and the consistent omission of all controversial material has made the volume even more concise than before. In the treatment of the "newer" diseases, such as ruptured intervertebral disc, a conservative approach is taken. Continued emphasis of the pathogenesis is seen. There is a substantial increase in the number of tables and illustrations, many of which are either original or have been taken from most reliable sources. The bibliography of each chapter has been revised and augmented by many new references.

The value of this textbook as a basic reference for student and practitioner has been definitely increased by virtue of this revision.

J. A. W.

Vitamins and Hormones. Vol. I. Advances in Research and Applications. Edited by Robert S. Harris and Kenneth V. Thimann. With a Foreword by E. V. McCollum. 452 pages; 23.5 × 15.5 cm. Academic Press, Inc., New York City. 1943. Price, $6.50.

This volume begins a new review series designed to correlate various aspects of research in the field of vitamins and hormones. No attempt has been made to cover the entire field, but ten subjects are rather exhaustively treated by well qualified investigators. The chapter titles include the following: Choline-Chemistry and Significance as a Dietary Factor, The Appraisal of Nutritional States, Physical Methods for the Identification and Assay of Vitamins and Hormones, The Chemistry and Physiological Relationship between Vitamins and Amino Acids, The Photoceptor Function of the Carotenoids and Vitamin A, The Significance of the Vitamin Content of Tissues, Growth-Factor for Protozoa, Physiology of Anti-Pernicious Anemia Material, The Intermediate Metabolism of the Sex Hormones, and The Hormones of the Adrenal Cortex. Each chapter is carefully outlined both in the table of contents and at the beginning of the chapter, thus facilitating reference to subtopics. Extensive references appear at the end of each chapter, and there is an author and subject index.

This series should become more and more valuable as a comprehensive reference with each succeeding annual volume.

M. A. A.

BOOKS RECEIVED

Books received during October are acknowledged in the following section. As far as practicable, those of special interest will be selected for review later, but it is not possible to discuss all of them.

Clinical Diagnosis by Laboratory Examinations. By JOHN A. KOLMER, M.S., M.D., Dr.P.H., Sc.D., LL.D., L.H.D., F.A.C.P. 1239 pages; 25 × 17.5 cm. 1943. D. Appleton-Century Company, Inc., New York. Price, $8.00.

A Clinical and Experimental Investigation of the Blood Cholesterol Content in Myxoedema and Other Conditions. By E. H. STOKES, M.B., Ch.M. (Sydney), F.R.A.C.P. 121 pages; 25 × 18.5 cm. 1941. Australasian Medical Publishing Company Limited, Sydney, Australia. (Accepted as a thesis for admission to the degree of Doctor of Medicine in the University of Sydney.)

Renewal Pages—Specialties in Medical Practice. Edited by EDGAR VAN NUYS ALLEN, M.D. 270 pages; 24.5 × 18.5. 1943. Thomas Nelson and Sons, New York. Price, $5.40 per set.

Biological Symposia. Volume X: Frontiers in Cytochemistry. Edited by JAQUES CATTELL. 334 pages; 25 × 17.5 cm. 1943. Jaques Cattell Press, Lancaster, Pennsylvania. Price, $3.50.

Peripheral Vascular Diseases (Angiology). By SAUL S. SAMUELS, A.M., M.D. 84 pages; 22 × 14.5 cm. 1943. Oxford University Press, New York. Price, $2.00.

Proctology. By SYLVAN D. MANHEIM, M.D. 137 pages; 22 × 14.5 cm. 1943. Oxford University Press, New York. Price, $2.00.

China's Health Problems. By DR. SZEMING SZE (General Secretary, Chinese Medical Association; Editor, Chinese Medical Journal). 60 pages; 23.5 × 16 cm. 1943. Chinese Medical Association, Washington, D. C. Price, $1.00.

Anales del Instituto de Medicina Experimental de Valencia. Tomo 1. Fasciculo 1. 237 pages; 21 × 15.5 cm. 1943. Editorial F. Domenech, S.A., Valencia.

Irrigacion Normal del Nodulo de Keith y Flack, Tawara, Haz de His y Sus Ramas. Estudio Previo de la Distribucion de los Gruesos Vasos Coronarios Cardiacos. By DR. EDUARDO F. LASCANO. 100 pages; 27 × 18.5 cm. 1942. El Ateneo, Buenos Aires, Argentina.

The Medical Use of Sulphonamides. Medical Research Council—War Memorandum No. 10. 46 pages; 24.5 × 15.5 cm. 1943. His Majesty's Stationery Office, London, England. Price, 9d. net.

Manometric Methods as Applied to the Measurement of Cell Respiration and Other Processes. 2nd Edition. By MALCOLM DIXON, Ph.D., Sc.D., F.R.S. With a Foreword by SIR F. G. HOPKINS, O.M., F.R.S. 157 pages; 19.5 × 13.5 cm. 1943. The Macmillan Company, New York City. Price, $1.75.

COLLEGE NEWS NOTES

Additional A. C. P. Life Members

The College is gratified to announce that Dr. Emry G. Hyatt, F.A.C.P., Tulsa, Okla., and Dr. Raymond Sands, F.A.C.P., Santa Monica, Calif., became Life Members of the American College of Physicians on November 23, 1943, having subscribed the amount designated in the By-laws, said payments having been added to the permanent Endowment Fund of the College.

Gifts to the College Library

We gratefully acknowledge receipt of the following gifts to the College Library of Publications by Members:

Books

Dr. Alexander S. Wiener (Associate), Brooklyn, N. Y.—"Blood Groups and Transfusion."

Reprints

J. Heinz Ahronheim (Associate), Captain, (MC), AUS—1 reprint;
Dr. Frank N. Allan, F.A.C.P., Boston, Mass.—1 reprint;
Dr. Russell S. Anderson, F.A.C.P., Erie, Pa.—1 reprint;
Dr. Arthur J. Atkinson (Associate), Chicago, Ill.—8 reprints;
Dr. Andrew L. Banyai, F.A.C.P., Wauwatosa, Wis.—2 reprints;
H. Dumont Clark (Associate), Major, (MC), AUS—1 reprint;
Dr. Oscar G. Costa-Mandry, F.A.C.P., Santurce, San Juan, P. R.—1 reprint;
Daniel B. Faust, F.A.C.P., Colonel, (MC), U. S. Army—1 reprint;
Harold J. Harris, F.A.C.P., Lieutenant Commander, (MC), U. S. Naval Reserve—1 reprint;
Dr. Herbert T. Kelly, F.A.C.P., Philadelphia, Pa.—2 reprints;
Dr. Arthur B. Landry, F.A.C.P., Hartford, Conn.—1 reprint;
Charles S. Mudgett, F.A.C.P., Colonel, (MC), U. S. Army—1 reprint;
Dr. Foster Murray, F.A.C.P., Brooklyn, N. Y.—1 reprint;
Dr. Franklin B. Peck, F.A.C.P., Indianapolis, Ind.—2 reprints;
Dr. Earle W. Phillips, F.A.C.P., Phoenix, Ariz.—2 reprints;
Walter L. Voegtlin (Associate), Lieutenant Commander, (MC), U. S. Naval Reserve 1 reprint;
Charles E. Watts, F.A.C.P., Captain, (MC), U. S. Naval Reserve—1 reprint;
Dr. Alexander S. Wiener (Associate), Brooklyn, N. Y.—7 reprints;
Dr. Salvador Zubiran, F.A.C.P., Mexico City, D. F.—2 reprints.

Additional A. C. P. Members in the Armed Forces

Already published in preceding issues of this journal were the names of 1,489 Fellows and Associates of the College on active military duty. Herewith are reported the names of 12 additional members, bringing the grand total to 1,501.

M. Meredith Baumgartner
William C. Dine
Thomas H. Ham
George J. Kastlin
Leslie R. Kober
Robert P. McCombs
Alphonse McMahon
Gilberto S. Pesquera
Albert Soiland
Arthur S. Strauss
George W. Weber
G. Stuart Wilson

The following members of the American College of Physicians have either retired or have been honorably discharged for physical disability from active service in the armed forces:

Major W. Osler Abbott, (MC), AUS, Philadelphia, Pa.—discharged, 9/28/42; deceased, 9/10/43.
Lieutenant Commander Douglas D. Baugh, (MC), USN, Columbus, Miss.—discharged, 12/18/42.
Captain Michael Bernreiter, (MC), AUS, Kansas City, Mo.—discharged, 7/11/43.
Lieutenant (jg) George A. Cann, (MC), USNR, Reno, Nev.—retired, 4/20/43.
Lieutenant Colonel Harold Archibald DesBrisay, RCAMC, Vancouver, B. C., Can.—discharged, October, 1942.
Captain Paul D. Foster, (MC), AUS, Los Angeles, Calif.—discharged, 2/3/43.
Lieutenant Colonel Ben R. Heninger, (MC), AUS, New Orleans, La.—discharged, 1/31/43.
Lieutenant Commander James J. Hennessy, (MC), USNR, Hartford, Conn.—discharged, 4/10/43.
Major Edwin P. Kolb, (MC), AUS, Holtsville, N. Y.—retired, 11/6/42.
Captain Milton M. Portis, (MC), California State Guard, Beverly Hills, Calif.—retired to inactive list, 4/15/43.
Captain H. Milton Rogers, (MC), AUS, St. Petersburg, Fla.—discharged, 10/15/43.
Lieutenant Colonel James F. Rooney, (MC), AUS, Albany, N. Y.—discharged, 5/28/41.
Lieutenant Commander Ralph L. Shanno, (MC), USNR, Forty Fort, Pa.—discharged, 11/1/42.
Lieutenant Commander Walter C. Smallwood, (MC), USNR, Long Beach, Calif.—discharged, 5/15/42.
Edwin E. Ziegler, U. S. Public Health Service, Bethlehem, Pa.—resigned, 9/8/42.

New College Membership Roster

In accordance with directions of the Executive Committee of the Board of Regents, the American College of Physicians has forgone the publication of a complete membership directory for 1943, but it has published a full "Membership Roster," which includes the listing of Associates, Fellows and Masters as of August, 1943. This publication was mailed to all members in good standing early in November, with the exception of those members who are on overseas military service. A copy will be held for such members, subject to delivery at their request.

Next Examinations, American Board of Internal Medicine

The next written examination of the American Board of Internal Medicine will be held February 21, 1944. The Assistant Secretary-Treasurer, Dr. William A. Werrell, 1301 University Ave., Madison 5, Wis., announced that applications for admission to the examination should be filed early in December, before December 15, if possible. More leeway will be granted to candidates on military duty and a special effort will be made to accommodate them at the examinations.

Announcement, Directory of Medical Specialists

The Directory of Medical Specialists will be published by the A. N. Marquis Company of Chicago, publishers of "Who's Who in America." Previous editions

were published by the Columbia University Press of New York City. The next edition will appear in 1945, but supplemental lists of those certified by American Boards since the last edition of the Directory, 1942, will be published.

Dr. Paul Titus of Pittsburgh will continue as the Directing Editor and Dr. J. Stewart Rodman of Philadelphia will continue as Associate Editor. The Editorial Board is composed of the Secretaries of the fifteen American Boards. Communications should be addressed to the Directing Editor, Directory of Medical Specialists, 919 N. Michigan Ave., Chicago 11, Ill.

Dr. Parley Nelson (Associate), Rexburg, Idaho, has been elected President of the Idaho State Medical Association for the coming year.

Captain Norman L. Murray (Associate), (MC), AUS, stationed with the Air Force at Gowen Field, Boise, Idaho, addressed the Southwestern Idaho District Medical Society on October 21, 1943. His subject was "Office Management of the Diabetic." Captain Murray is formerly of New Jersey.

Dr. Howard Wakefield, F.A.C.P., Chicago, Ill., spoke on "Acute and Chronic Coronary Occlusion" at a meeting of the Du Page County Medical Society in Elmhurst, Ill., on November 17, 1943.

Dr. Walter E. Macpherson (Associate), of Los Angeles, Calif., is the President of the College of Medical Evangelists.

On November 10, 1943, Dr. Herbert T. Kelly, F.A.C.P., Philadelphia, Chairman of the Committee on Nutrition of the Medical Society of the State of Pennsylvania, addressed the First Regional Pennsylvania Health Institute, Erie, Pa., on the subject, "Improving Nutrition of all the People." The meeting was held under the auspices of the Pennsylvania State Department of Health.

Dr. Frank N. Allan, F.A.C.P., Boston, Mass., addressed a District Meeting of the Ontario Medical Society in Brantford, Ont., Can., on October 6, 1943. His subject was "Why Do People Feel Weak and Tired? Differential Diagnosis and Treatment."

Dr. Edward J. Stieglitz, F.A.C.P., Washington, D. C. addressed the 8th Annual Meeting of the Industrial Hygiene Foundation at Pittsburgh, November 11, on "Health Problems of the Older Employee and Employer."

Dr. George E. Baker, F.A.C.P., Casper, Wyo., delivered an address on "Rocky Mountain Spotted Fever; an Increasing Hazard: Diagnosis and Treatment," before the Chicago meeting of the Inter-State Post Graduate Medical Association of North America, October 26, 1943.

American Medical Association to Resume Annual Sessions

The Journal of the American Medical Association in a recent issue announced that its annual session will be held in Chicago, June 12–16, 1944. The meetings of the House of Delegates will be held at the Palmer House and the scientific exhibit will be installed there. However, the technical exhibit will be housed at the Stevens Hotel.

Wisconsin State Medical Society Announces Dates for Annual Meeting

The State Medical Society of Wisconsin will hold its 1944 session September 18–20 in Milwaukee. The above announcement is made in an effort to encourage other societies to avoid conflicts in meeting dates.

Course in Hospital Administration

Northwestern University, Chicago, through a grant received from the Johnson & Johnson Research Foundation, has initiated a course in hospital administration with an enrollment of thirty-nine students, only eight of whom who are not connected with a hospital. Of the eight persons not associated with a hospital, two are employed on hospital magazines, two are physicians, one is director of a hospital council and one is employed by the American College of Surgeons.

Western Reserve University School of Medicine Celebrates Its One Hundredth Anniversary

Western Reserve University School of Medicine, Cleveland, Ohio, celebrated its One Hundredth Anniversary, October 27, 1943. Dr. Howard T. Karsner, F.A.C.P., Cleveland, was the official representative of the American College of Physicians on this occasion.

At 11:30 a.m., Dr. George H. Whipple addressed an audience of about 600 on the subject of "Blood Plasma Proteins—Their Production, Function, Substitution and Replacement." He outlined with great clarity the progress that has been made in the scientific study of the utilization of amino acids and of whole plasma in connection with the building of hemoglobin and the liberation of proteins into the circulation. Immediately following, a luncheon was given by the University to delegates to the celebration, delegates to the Association of American Medical Colleges, and guest speakers of the celebration and of the meetings of the Association. At 3:30 p.m., the University Convocation was attended by about 150 delegates from universities, colleges, medical societies and philanthropic foundations. A guard of honor was

formed by medical students representing both Army and Navy. President W. G. Leutner presided, and addresses were delivered by Dr. Howard T. Karsner and Dr. Alan Gregg of the Rockefeller Foundation. Dr. Gregg's address, "The Matrix of Medicine," was a scholarly approach to the situation of Medicine in relation to educational, cultural and other matrices in which Medicine finds itself. He suggested that a non-political national committee be organized to make recommendations concerning the future of medical practice and education. In the evening a dinner was given by the University, attended by delegates, members of the faculties and alumni. About 400 were present and were addressed by Dr. Reginald Fitz of the Harvard Medical School. The title of his address, "The Crimson Thread," was developed so that the various interchanges of ideas and of personnel between the School of Medicine in Cleveland and the Harvard Medical School were brought out in interesting and entertaining fashion.

On the morning of the following day, scientific addresses were made to the alumni by graduates of the School who have attained distinction in various parts of the country. The Commencement for the Medical School was held in the afternoon and in the evening the principal address at the Alumni dinner was by Frederick C. Waite, Emeritus Professor of Histology and Embryology, who showed clearly the influence of the School on various community activities.

Report on Regional Meeting in Seattle

The first Regional Meeting of the American College of Physicians to be held in the Northwest was conducted at Seattle, Washington, Friday, September 24, 1943, and included the territory of Washington, Oregon, Idaho, Alberta, British Columbia, Manitoba and Saskatchewan. The meeting was eminently successful; the program was superior and the attendance was greater than anticipated. The medical population in that area is not nearly so dense as in many other parts in this country and Canada, and consequently the number of members of the College is small in comparison with more densely populated areas. Fifty per cent of all College Fellows and Associates were in attendance, a percentage not yet reached by any other area of the country at a Regional Meeting. In addition, there were 92 guests including 14 officers from the Royal Canadian Army Medical Corps, 2 officers from the Royal Canadian Navy Medical Corps, 34 officers from the U. S. Army Medical Corps, 18 officers from the U. S. Navy Medical Corps, 2 officers from the U. S. Public Health Service and 22 civilian physicians.

Dr. Edwin G. Bannick, Acting Governor for Washington, was the General Chairman, and was ably assisted by Dr. Homer P. Rush, College Governor for Oregon; Dr. Samuel M. Poindexter, Acting Governor for Idaho; and Dr. George F. Strong of Vancouver, Governor for the Southwestern Provinces of Canada. These Governors in turn were ably aided by active committees in each state and province.

Report on Regional Meeting in Chicago

A Regional Meeting of the College for Illinois, Indiana, Iowa, Michigan and Wisconsin was held at the Drake Hotel, Chicago, Saturday, October 16, 1943, under the General Chairmanship of Dr. LeRoy H. Sloan, Governor for Northern Illinois, and the active participation of Dr. Cecil M. Jack of Decatur, Governor for Southern Illinois; Dr. Robert M. Moore, Governor for Indiana; Dr. B. F. Wolverton of Cedar Rapids, Governor for Iowa; Dr. P. L. Ledwidge of Detroit, Acting Governor for Michigan; and Dr. Elmer L. Sevringhaus of Madison, Governor for Wisconsin.

This Regional Meeting concluded a week devoted to a postgraduate course in Endocrinology under the auspices of the College at the Presbyterian Hospital, directed by Dr. Willard O. Thompson. In this course, there were registered 78 different physicians, mostly Fellows and Associates of the College and Medical Officers of the Armed Forces. No activity ever conducted by the College received more expressions of appreciation and commendation than this course.

On Friday evening, October 15, the entire group from the Postgraduate Course, with a faculty selected by the College and by the Committee on War-Time Graduate Medical Meetings, went to the Great Lakes Naval Hospital where a program of postgraduate lectures was presented to Medical Officers at that station and other Medical Officers from Army installations from the surrounding territory. About 250 were in attendance.

The official Regional Meeting of the College followed on Saturday, October 16 at the Drake Hotel in Chicago. The program has already been published in a previous issue of this journal. There were 222 members of the College in attendance, or 36.3 per cent of the members from the territory represented. In addition, there were 130 guests, including 64 Medical Officers from the Army and Navy and Public Health Service and 66 non-member civilian physicians. The session was concluded with a dinner meeting in the evening at which approximately 300 were in attendance. The dinner meeting speakers included Dr. Charles H. Cocke, Asheville, N. C., First Vice President of the College; Dr. Ernest E. Irons, Chicago, Ill., President-Elect of the College; Brigadier General Hugh J. Morgan, (MC) U. S. A., Washington, D. C.; Dr. Willard O. Thompson, Chicago, Ill.; and Mr. E. R. Loveland, Philadelphia, Pa., Executive Secretary. Governor Sloan was the Toastmaster.

A. C. P. Fellows Honored at Meeting of Association of Military Surgeons

At the annual dinner of the Association of Military Surgeons of the United States at Philadelphia, October 22, 1943, Navy Night, the Gorgas Medal was awarded to Dr. Hugh S. Cumming, F.A.C.P., former Surgeon General of the U. S. Public Health Service. This award was founded by John Wyeth & Brother. Captain Louis H. Roddis, F.A.C.P., (MC), U. S. Navy, was awarded the Wellcome Medal, established by Sir Henry Wellcome.

A. C. P. Regional Meeting Held in Philadelphia

A Regional Meeting of the American College of Physicians for Eastern Pennsylvania, Delaware, New Jersey and Eastern New York was held in Philadelphia, November 19, 1943, under the Chairmanship of Dr. Edward L. Bortz (Commander, MC, U. S. N. R.), Governor for Eastern Pennsylvania, and the active participation of the College Governors for the territory, namely; Dr. Lewis B. Flinn, Governor for Delaware; Dr. George H. Lathrope, Governor for New Jersey; and Dr. Asa L. Lincoln, Governor for Eastern New York. The Regional Meeting program terminated a two-weeks postgraduate course in Special Medicine, conducted by the College for its members and for medical officers in the armed forces, at Philadelphia Institutions under the Directorship of Dr. Charles L. Brown, F.A.C.P., Professor of Medicine at Temple University.

An analysis of the attendance at the Regional Meeting appears below. This probably was one of the largest Regional Meetings the College has held and it was the consensus that this meeting was one of the best in the College history.

A. By geographical distribution:

	% of Membership	Members	Guests	Total
Eastern Pennsylvania	42.5	113	80	193
Delaware	41.6	5	4	9
New Jersey	27.1	31	20	51
Eastern New York	6.2	40	8	48
Other States		64	15	79
Canada		3	1	4
		256	128	384

B. By class:

Fellows	Associates	Guests	Total	RCAMC	(MC)USA
192	64	128	384	3	52

(MC)USN	USPHS	Civilian
21	6	302

25% of the A. C. P. members in the territory of this Regional Meeting was in attendance.

The program was as follows:

MORNING SESSION—9:30 a.m.

Hospital of the University of Pennsylvania

Presiding Officer

O. H. PERRY PEPPER, M.D., F.A.C.P.

9:30 "Hypoprothrombinemia."
DR. FRANKLIN D. MURPHY.

9:45 "Differentiation of Functional Hypoglycemia from That Due to Adenoma of the Pancreas."
DR. FRANCIS D. W. LUKENS.

10:00 "Case of Toxoplasmic Encephalomyelitis."
DR. JAMES WENDELL.

10:15 "Statistics on Medical Treatment of Bleeding Ulcer."
DR. T. GRIER MILLER.

10:30 "Demonstration of a Small Oxygen Tent."
DR. LINCOLN GODFREY, JR.

10:40 "The Case for Trial of Castration in Diffuse Lupus Erythematosis."
DR. EDWARD ROSE.

11:00 "Gelatin as a Blood Substitute."
DR. C. EVERETT KOOP.

11:15 "The Virus Encephalitides."
DR. GEORGE D. GAMMON.

11:35 "Comments on Hemoglobinuria."
DR. WILLIAM C. STADIE.

11:45 "Electrocardiographic Interpretation."
DR. CHARLES C. WOLFERTH.

LUNCHEON

12:30 p.m.

COLLEGE HEADQUARTERS

4200 Pine Street, Philadelphia, Pa.

AFTERNOON SESSION—3:00 p.m.
Ballroom, Benjamin Franklin Hotel

Presiding Officer
GEORGE H. LATHROPE, M.D., F.A.C.P.
Governor for New Jersey

1. "Medicine Overseas."
   HUGH J. MORGAN, M.D., F.A.C.P., Brigadier General, (MC), U. S. Army, Professional Service Division, Office of the Surgeon General, Washington, D. C.
2. "The Management of Hyperthyroidism."
   DAVID P. BARR, M.D., F.A.C.P., Professor of Medicine, Cornell University Medical College, New York, N. Y.
3. "Effort Syndrome and Allied Conditions in Civil and Military Practice."
   JONATHAN C. MEAKINS, M.D., F.A.C.P., Brigadier, R.C.A.M.C., Director General of Medical Services of Canada, Ottawa, Ont.

INTERMISSION

Presiding Officer
ASA L. LINCOLN, M.D., F.A.C.P.
Governor for Eastern New York

4. "Medical Problems of the Middle East."
   CRAWFORD F. SAMS, M.D. (by invitation), Colonel, (MC), U. S. Army, Medical Field Service School, Carlisle Barracks, Carlisle, Pa. (Recently returned from Cairo.)
5. "Medical Problems in an Army General Hospital."
   MARSHALL N. FULTON, M.D., F.A.C.P., Lieutenant Colonel, (MC), U. S. Army, Chief of Medical Service, Valley Forge General Hospital, Phoenixville, Pa.
6. "Medicine with the Marines in Action."
   DON S. KNOWLTON, M.D., F.A.C.S. (by invitation), Captain, (MC), U.S.N.R., Camp Surgeon, Camp Lejeune, New River, N. C. (Action in South Pacific with First Marine Division.)

PROBLEMS CONVIVIAL
6:30 p.m.—Cocktails
Washington Room, Mezzanine Floor
Benjamin Franklin Hotel
7:15 p.m. Dinner—(Informal)
Ballroom, Benjamin Franklin Hotel
Toastmaster, GEORGE MORRIS PIERSOL

Official envoys of the Surgeons General of the United States were Brigadier General Hugh J. Morgan, U. S. Army, Captain Joseph A. Biello, District Medical Officer of the Fourth Naval District, U. S. Navy, Dr. R. C. Williams, Medical Director, District No. 1, U. S. Public Health Service.

Brief addresses were also made by Dr. Charles H. Cocke, First Vice President of the College, Asheville, N. C.; Brigadier Jonathan C. Meakins, Director General

of Medical Services of Canada, Ottawa; Commander Edward L. Bortz, (MC), U.S.N.R., A. C. P. Governor for Eastern Pennsylvania; Dr. O. H. Perry Pepper, F.A.C.P., President of the College of Physicians of Philadelphia, and Mr. E. R. Loveland, Executive Secretary of the College.

Among distinguished guests at the dinner meeting were members of the Board of Regents, Dr. William B. Breed, Boston, Chairman of the Board of Governors, Dr. Chauncey W. Dowden, Louisville, Vice-Chairman of the Board of Governors, Dr. Nelson G. Russell, Sr., Buffalo, Governor for Western New York, Dr. Alex. M. Burgess, Providence, Governor for Rhode Island, College Governors for the participating States, the Deans of all medical schools in Philadelphia, Dr. Hubley Owen, Director of Public Health of Philadelphia, Captain Jesse W. Allen, Commanding Officer of the U. S. Naval Hospital at Philadelphia, and Captain Clarence J. Brown, Executive Officer of the U. S. Naval Hospital of Philadelphia.

Elections to Fellowship and Associateship

At a meeting of the Board of Regents of the American College of Physicians at Philadelphia, Pa., November 20, 1943, the following candidates were officially elected to the class of membership indicated:

Elected to Fellowship

Adcock, John Delbert, Ann Arbor, Mich.
Ahronheim, J(acques) Heinz, Jackson, Mich. (AUS)
Allen, Lewis George, Kansas City, Kan.
Andujar, John Jose, Fort Worth, Tex.
Applebaum, Irving Loren, Newark, N. J. (AUS)
Ashby, John Edmund, Dallas, Tex.
Baganz, Crawford Norbert, Lyons, N. J. (USNR)
Ballmer, Robert Sidney, Midland, Mich.
Bell, Irving Russell, Edmonton, Alta., Can.
Bernstein, Arthur, Newark, N. J.
Bernstein, Benjamin Maurice, Brooklyn, N. Y.
Blalock, Joseph Rogers, Marion, Va.
Blankenhorn, Marion Arthur, Cincinnati, Ohio
Bloch, W(illiam) Austin, Louisville, Ky.
Blount, Rankin Clay, Lexington, Ky. (AUS)
Bohnengel, Charles Andrew, New York, N. Y. (AUS)
Bradford, William Hartsel, Dallas, Tex.
Brown, Omar Jesse, (MC), U. S. Navy
Byne, James Miller, Jr., Waynesboro, Ga.
Callomon, Verner Bickart, Pittsburgh, Pa.
Campbell, Eugene Paul, Philadelphia, Pa.
Carabelli, A(milcare) Albert, Trenton, N. J. (AUS)
Choate, Allyn Blythe, Charlotte, N. C.
Clark, H(arry) Dumont, Denver, Colo. (AUS)
Cleveland, Donald Ernest Howell, Vancouver, B. C., Can.
Cohen, Sumner S., Oak Terrace, Minn.
Conn, Jerome W., Ann Arbor, Mich.
Corlette, Marvin Brown, Pasadena, Calif. (AUS)
Crowell, Lester Avant, Jr., Lincolnton, N. C.
Davenport, Walter Paul, (MC), U. S. Army
DeArmond, (Albert) Murray, Indianapolis, Ind. (AUS)
Delarue, Edward Arthur, Jr., Richmond, Va. (AUS)

Delp, Mahlon Henry, Kansas City, Kan. (AUS)
Easom, Herman Franklin, Wilson, N. C.
Edwards, Joseph Castro, St. Louis, Mo. (AUS)
Eisner, Eugene A., New York, N. Y. (USNR)
Ershler, Irving, Binghamton, N. Y. (AUS)
Felson, Henry, Cincinnati, Ohio (AUS)
Ferris, Caryl Ray, Kansas City, Mo.
Friedenson, Meyer, New York, N. Y. (AUS)
*Gais, Elmer Stewart, New York, N. Y. (AUS)
Gammon, George Davis, Philadelphia, Pa.
Garvin, Curtis Ferbert, Cleveland, Ohio
Geeslin, Lawrence Easter, Atlanta, Ga. (AUS)
Goehl, Reinhold O., Grand Forks, N. D.
Grollman, Arthur, Winston-Salem, N. C.
Halley, Charles Robert Lee, Washington, D. C.
Halpin, Frank William, Fort Worth, Tex. (AUS)
Harper, Harry Taylor, Jr., Augusta, Ga.
Harrison, Meyer Max, Louisville, Ky. (AUS)
Harvill, T(homas) Haynes, Dallas, Tex. (USNR)
Haynes, Elmer, Madison, Wis.
Hernandez-Morales, Federico, San Juan, P. R.
Higgins, William Harrison, Richmond, Va.
Holbrook, Arthur Andrews, Milwaukee, Wis. (AUS)
Jacobs, Sydney, New Orleans, La.
Jennes, Sidney Weinberg, Waterbury, Conn. (AUS)
Johnston, Elbridge Eugene, St. Johnsbury, Vt.
Jordan, William Riely, Richmond, Va.
Kelly, Frank Brazzil, Chicago, Ill.
Kilgore, F(ranklin) Hartman, Houston, Tex.
Kirk, Norman Thomas, (MC), U. S. Army
Kline, Edward Mahon, Cleveland Heights, Ohio
Knight, Alva Allan, Chicago, Ill.
Koppe, Harold Fredrick, Dayton, Ohio
Leedham, Charles Laurn, (MC), U. S. Army
LeFor, Frank George, Yakima, Wash.
Leopold, Henry Nathan, San Antonio, Tex.
Levy, Jerome Sickles, Little Rock, Ark. (AUS)
Levy, Robert Charles, Chicago, Ill. (AUS)
Lineberry, E(llis) Dice, Birmingham, Ala.
Lippschutz, Eugene John, Buffalo, N. Y. (USNR)
Loveman, Adolph Bernard, Louisville, Ky. (AUS)
Luchi, Angelo Luigi, Wilkes-Barre, Pa.
Lusk, Frank B., Chicago, Ill. (AUS)
MacBryde, Cyril Mitchell, Clayton, Mo.
MacNeal, Perry Scott, Philadelphia, Pa.
Macpherson, Walter Everett, Los Angeles, Calif.
Martin, John Walter, Jr., Cleveland, Ohio (USNR)
Martin, Louis Everett, Los Angeles, Calif.
Matthews, Edward de Saunhac, New Orleans, La. (AUS)
Matthews, Morgan Whitsitt, Shreveport, La.
Mignone, Joseph, New Haven, Conn. (USNR)
Minter, Merton Melrose, San Antonio, Tex.
Morgan, John Russell Egbert, Vancouver, B. C., Can. (RCAMC)

* Advancement to Fellowship as of April, 1944.

Morrison, Maurice, Brooklyn, N. Y.
Neff, Walter Scott, Virginia, Minn.
O'Brien, George Francis, Chicago, Ill. (AUS)
Ogaard, Adolph Thompson, New Orleans, La. (AUS)
Page, Irvine Heinly, Indianapolis, Ind.
Pendergrass, Eugene Percival, Philadelphia, Pa.
Penner, Abraham, New York, N. Y. (AUS)
Pernokis, Evans William, Chicago, Ill. (USNR)
Peters, Frank Hart, New York, N. Y.
Pleyte, Arthur A., Milwaukee, Wis.
Powers, Bruce Rankins, Knoxville, Tenn.
Quinlan, J(ames) William, Rochester, N. Y. (USNR)
Reich, Nathaniel Edwin, Brooklyn, N. Y.
Rothrock, Henry Abraham, Jr., Bethlehem, Pa. (USNR)
Schmitt, George Fredrick, Jr., Rochester, Minn. (USNR)
Sc[illegible]itker, Maurice Arthur, Toledo, Ohio (AUS)
Segal, Harry L., Rochester, N. Y.
Shiflett, Emory Lee, Louisville, Ky.
Slagle, George Willard, Battle Creek, Mich. (USNR)
Smith, Frank Edward, Jr., New York, N. Y. (USNR)
Smith, Joseph Alphonsus, Metuchen, N. J.
Solomon, Walter Maximilian, Cleveland, Ohio (AUS)
Steele, Brandt Ferguson, Indianapolis, Ind. (AUS)
Steuer, Leonard Gerard, Cleveland, Ohio (AUS)
Stuppy, George William, Chicago, Ill. (AUS)
Swartz, Frederick Charles, Lansing, Mich. (AUS)
Teitelbaum, Myer, Detroit, Mich. (AUS)
Temple, R(ufus) Henry, Kinston, N. C. (AUS)
Thompson, J(oseph) Lawn, Jr., Washington, D. C. (AUS)
Tumen, Henry Joseph, Philadelphia, Pa.
Vaughn, Louis Dysart, Rochester, Minn. (AUS)
Vorzimer, Jefferson Jonas, New York, N. Y.
Waddill, J(ames) Franklin, Norfolk, Va. (AUS)
Walsh, John Joseph, Pottsville, Pa.
Wardrip, Buford Haven, San Jose, Calif.
Warren, Charles Ford, Brooklyn, N. Y.
Warren, Daniel Davis, Waco, Tex.
Way, Karl Duren, Akron, Ohio
Wiener, Alexander Solomon, Brooklyn, N. Y.
Wilfong, Clavel Tyrus, Roanoke, Va.
Wirtschafter, Zolton Tillson, Cleveland, Ohio (AUS)

ELECTED TO ASSOCIATESHIP

Adams, M. Vaun, Mobile, Ala.
Agerty, Horst Albert, Merion, Pa. (AUS)
Anderson, Forrest Nelson, Los Angeles, Calif. (AUS)
Archinard, John Joseph, New Orleans, La. (AUS)
August, Myron, Cleveland, Ohio
Babey, Andrew Michael, Brooklyn, N. Y.
Baker, Lynne Elmer, Jacksonville, Fla. (USNR)
Baker, Russel Lobach, Gaston, Ore. (AUS)
Ballinger, Joseph, New York, N. Y.
Barbato, Lewis, San Antonio, Tex. (AUS)

Beck, Luther Clagett, Honolulu, T. H.
Benenson, William Osler, Napanoch, N. Y. (AUS)
Benton, Louis Joseph, Ogdensburg, N. Y. (AUS)
Best, Gorden Newall, Council Bluffs, Iowa
Boland, Edward Ward, Los Angeles, Calif. (AUS)
Boylston, George Arthur, Wilmette, Ill. (AUS)
Bronstein, Lewis Herman, New York, N. Y. (AUS)
Burgert, Paul Haskell, Lake Forest, Ill.
Burney, Leroy Edgar, U. S. Public Health Service
Buttorff, Gordon Stephen, Louisville, Ky.
Caldwell, David Martin, Pittsburgh, Pa.
Caldwell, Hayes Woodrow, Rochester, Minn. (AUS)
Campbell, Joseph Lester, Ulster, Pa. (AUS)
Candel, Samuel, Brooklyn, N. Y. (USNR)
Cannon, Edward Aloysius, North Bergen, N. J.
Carnicelli, Thomas John, Framingham, Mass.
Carpenter, Gurth, Los Angeles, Calif.
Carroll, Howard Bertram, Chicago, Ill.
Chester, William Patrick, Detroit, Mich.
Christie, Harry C., New York, N. Y.
Coggeshall, Howard Cranor, Boston, Mass. (AUS)
Crago, Felix Hughes, Great Falls, Mont. (AUS)
Cramer, Charles, Jackson Heights, N. Y.
Crane, A(ugust) Reynolds, Brooklyn, N. Y.
Davidge, Lucious Lamar, Shreveport, La. (AUS)
Davis, John Preston, Winston-Salem, N. C. (AUS)
Del Duca, Vincent P., Camden, N. J. (AUS)
Dublin, William Brooks, Fort Steilacoom, Wash.
Duncan, Charles Newton, Dallas, Tex. (USNR)
Dunn, William LeRoy, Washington, D. C.
Dyer, John Lewis, New Orleans, La. (AUS)
Eichert, Herbert, Jacksonville, Fla. (USNR)
Ellis, Mackinnon, Bryn Mawr, Pa. (USNR)
Engle, David Edwin, Elmhurst, Ill. (AUS)
Epstein, Samuel, Brooklyn, N. Y.
Fahlstrom, Stanley, Chicago, Ill. (AUS)
Ferry, John Lumice, Akron, Ind. (AUS)
Foltz, Eliot Eugene, Chicago, Ill.
French, A(dam) James, Ann Arbor, Mich. (AUS)
Garry, Mark William, Milwaukee, Wis.
Gettelfinger, Wilfrid Charles, Louisville, Ky.
Gillespie, Delmar Robert, Rochester, Minn. (AUS)
Gilmour, Monroe Taylor, Charlotte, N. C.
Greenwood, Edward David, Topeka, Kan. (AUS)
Guthrie, Morris Baker, Columbus, Ohio (AUS)
Hackler, Robert Hardin, Jr., Washington, N. C.
Hall, William Earle Brandon, Port Huron, Mich.
Ham, George Caverno, Charlottesville, Va. (AUS)
Hamlin, Percy Gatling, Williamsburg, Va. (AUS)
Harrington, Peter Francis, Providence, R. I.
Hartwell, Alfred Stedman, Honolulu, T. H.
Heffner, Bain Lafayette, Boston, Mass. (AUS)
Hing, Ng William, Arecibo, P. R. (AUS)
Irvine, Jed Hotchkiss, New York, N. Y.

Jacobson, Samuel Maurice, Cumberland, Md.
Janjigian, Edward Rupen, Danville, Pa. (AUS)
Kennedy, J(ames) Allen, Nashville, Tenn. (AUS)
Keveney, John Joseph, Philadelphia, Pa. (AUS)
Kneedler, William Harding, Philadelphia, Pa.
Kubanek, Joseph Louis, Eloise, Mich.
Landau, Frederick Louis, Jr., Bronxville, N. Y. (AUS)
Laney, Richard Paul, Skowhegan, Maine (AUS)
Learn, G(eorge) Emerson, Mt. Morris, N. Y.
Lehnhoff, Henry John, Rochester, Minn. (AUS)
Liggett, Robert Samuel, Denver, Colo. (AUS)
Lloyd, Leo Walter, Denver, Colo. (AUS)
Lohr, Oliver Willison, Saginaw, Mich.
Madison, Frederick William, Milwaukee, Wis.
Manning, Isaac Hall, Jr., Durham, N. C. (AUS)
Martin, Thomas Wilson, Pittsburgh, Pa. (AUS)
McEvoy, Francis Joseph, Royal Oak, Mich. (USNR)
McKean, George Thomas, Detroit, Mich. (AUS)
Midelfort, Christian Frederik, Eau Claire, Wis.
Mitchell, Robert Hartwell, Plainview, Tex. (AUS)
Modell, Walter, New York, N. Y.
Monto, Raymond Walter, Detroit, Mich. (AUS)
Murphy, Paul, St. Louis, Mo.
Muse, Joseph Ennalls, Jr., Baltimore, Md. (AUS)
Nicholson, William McNeal, Durham, N. C.
Ochs, Louis, Jr., New Orleans, La. (AUS)
Patton, Paul Bellmonte, Philadelphia, Pa. (AUS)
Peasley, Elmus Day, Raleigh, N. C. (AUS)
Peters, Carey Moss, Boston, Mass. (AUS)
Peters, Gustavus Alfred, Rochester, Minn.
Peters, Michael, Telford, Pa. (AUS)
Peterson, Heyes, Wheeling, W. Va. (USNR)
Power, Paul Herschell, Waco, Tex.
Rattigan, John Patrick, Brighton, Mass.
Revell, Samuel Thompson Redgrave, Jr., Baltimore, Md. (AUS)
Ropes, Marian Wilkins, Boston, Mass.
Ross, Edward Still, Dallas, Tex. (USNR)
Rotkow, Maurice Julian, Des Moines, Iowa (AUS)
Ruskin, Arthur, Galveston, Tex.
Saphir, William, Chicago, Ill. (AUS)
Scherlis, Sidney, Baltimore, Md. (AUS)
Schuck, Carl Alfred, St. Louis, Mo. (AUS)
Schultz, Arthur Francis, Newport, Ky. (AUS)
Senekjie, Harry Archak, New Orleans, La.
Shenson, Ben, San Francisco, Calif.
Shpiner, Leonard Benjamin, Boston, Mass. (AUS)
Siver, Robert Hutton, Cockeysville, Md.
Sokolov, Raymond A., Detroit, Mich.
Solovay, Hyman U., Brooklyn, N. Y. (AUS)
Spellberg, Mitchell Abraham, Chicago, Ill. (AUS)
Stone, Charles Frederic, Jr., Atlanta, Ga. (AUS)
Sunday, Stuart Dos Passos, Baltimore, Md. (AUS)
Swinny, Boen, San Antonio, Tex. (AUS)
Swirsky, Morgan Yale, New Haven, Conn.

Tesler, James, Brooklyn, N. Y.
Thomas, Lawrence Jay, Washington, D. C.
Vander Meer, Ray(mond), Grand Rapids, Mich. (AUS)
Vinal, Raymond Gould, Norwell, Mass. (AUS)
Von Schulz, Augustine Paul, Baltimore, Md.
Warrick, George Wilks, Birmingham, Ala. (AUS)
Warshawsky, Harry, West Lebanon, N. H.
Weinberg, Samuel Joseph, Los Angeles, Calif. (AUS)
White, Asher Abbott, Minneapolis, Minn.
Wiesel, Bertram Hirsh, Tuscaloosa, Ala.
Willett, Forrest Munroe, San Francisco, Calif. (AUS)
Willis, Charles Alfred, Birmingham, Ala.
Wilner, Paul Robert, Washington, D. C. (AUS)
Wilson, Charles Pearson, Portland, Ore.
Wilson, Walter Howard, Greenville, N. C. (AUS)
Wollenweber, Henry L., Baltimore, Md.
Woods, Robert Max, Milwaukee, Wis. (AUS)
Wright, Robert Broy, Baltimore, Md.
Zimmerman, Bruce, Seattle, Wash.
Zindler, George Alexander, Battle Creek, Mich.

A. C. P. to Have Election of Officers, 1944

At a meeting of the Board of Regents of the College, November 20, 1943, at Philadelphia, it was voted unanimously to hold a limited Annual Session in the Spring of 1944 for the chief purpose of electing Officers, Regents and Governors and to conduct an Annual Business Meeting. The date of the meeting will be announced at least one month in advance; it is probable that the meeting will be held in Philadelphia at the time of the customary Spring Meeting of the Board of Regents and of the Board of Governors.

SPECIAL NOTICE

A course in Electrocardiographic Interpretation for *graduate physicians* will be given at Michael Reese Hospital by Dr. Louis N. Katz, Director of Cardiovascular Research. The class will meet each week, starting Thursday, February 17, for 12 weeks, from 7:00 to 9:00 p.m.

Further information and a copy of the program may be obtained on application to the Cardiovascular Department, Michael Reese Hospital, Chicago, Ill.

OBITUARIES

DR. WILLIAM OSLER ABBOTT

Dr. William Osler Abbott, of Philadelphia, died at Waquoit, Massachusetts, on September 10, 1943. He was a victim of myelogenous leukemia. The diagnosis was made in May of 1942, within a week after his arrival, as a Major with the 20th General Hospital, at Camp Claiborne, Louisiana, his first assignment in the Army. On account of his affliction he was honorably discharged from the military service on the following September 28, but already before that time had decided to devote the rest of his life to an investigative attack on the disease that he had acquired. On his return to civil life and apparently with scant thought for his personal welfare, he threw himself into his new research problem with the same industry, enthusiasm and earnestness that he had previously displayed in his gastrointestinal investigations. He died in the midst of his hematological work, but fortunately, since it was sponsored by, and was a part of a larger investigative effort being conducted by the Memorial Hospital group in New York City, under the direction of Dr. Cornelius P. Rhoads, significant results to which he made some contribution may yet be obtained.

Dr. Abbott's more important contributions to medical knowledge, however, were in the field of gastroenterology. Following his graduation in 1928 from the University of Pennsylvania Medical School, he had his internship in the University Hospital, then became associated with the Gastrointestinal Section of the Medical Clinic of that institution, and in 1941 was made an Assistant Professor of Medicine in his Alma Mater. For three years (1931–34) he was also connected, on a part-time basis, with the University's Department of Pharmacology, where he secured invaluable training under the direction of Dr. A. N. Richards. This experience in physiology intensified his interest in the type of investigative work then underway in the Gastrointestinal Clinic and undoubtedly aided in his significant contributions to the development and the use of an intubation method for studies of intestinal function, and later, in coöperation with Dr. Charles G. Johnston, to the application of the new technique to patients with obstruction of the bowel. While the latter was his most dramatic and clinically useful accomplishment, his original studies on various aspects of the physiology of the human digestive tract are doubtless equally important. In all he published about forty papers on medical topics, most of them on the subject of small intestinal intubation, but he also was the author of a characteristically whimsical article on "The Problem of the Professional Guinea Pig" and, just before his death, of one on "Trends in Cancer Research."

He was the son of the late Dr. Alexander C. Abbott, a professor of bacteriology and of public health and hygiene at the University of Pennsylvania. His mother was a niece of Sir William Osler, whom Dr. Abbott resembled physically and in many of his other traits, especially in his whim-

sicality, versatility, and capacity for work. In spite of this he never referred to his greatuncle, preferring recognition only on the basis of personal accomplishments.

He was a member of most of the important national societies to which an internist is eligible: in addition to his Fellowship in this College, he was a member of the Society for Clinical Investigation, the American Clinical and Climatological Association, the American Gastroenterological Association and the Association of American Physicians. He also was a Fellow of the College of Physicians of Philadelphia and a member of the Charaka Club of New York and of the Interurban Clinical Society. He was largely responsible for the success of a combined "Exhibit on the Small Intestine," which, in 1935, received a "Special Certificate of Honor" from the American Medical Association, the "First Award" of the Radiological Society of North America and the "Gold Medal" of the American Roentgen Ray Society.

Dr. Abbott's tastes were simple. He loved nature and was an accomplished fisherman and sailor. His athletic interests were limited to fencing in college, where he was the local champion. He spent his leisure time with his family, and as much of it as possible on Cape Cod. His special interest in the natural sciences is indicated by the fact that, on preparing to leave for the Army, he secured various standard textbooks on geology, stating that he knew less about that particular science than any other. Indeed, even before he fell ill in Louisiana, he had described in letters to friends certain observations on the geological phenomena of that locality.

In all of Dr. Abbott's personal relationships he was quiet, stimulating and coöperative. He thought straight and was original, practical and scientific in his approach to all new problems. Under stress, as well as in the ordinary walks of life, he was efficient, resourceful and ingenious; and always, as was amply demonstrated in his final illness, he was courageous. He was a leader and an inspiration to all who worked with him. He will be sorely missed, not only by his family, to whom he was unusually devoted, but by a wide circle of friends and acquaintances, including especially many of the active clinical investigators throughout the country.

T. Grier Miller, M.D., F.A.C.P.

DR. JULIAN MAST WOLFSOHN

Dr. Julian Mast Wolfsohn died at Stanford University Hospital in San Francisco, California, July 1, 1943, following an operation for acute intestinal obstruction.

Dr. Wolfsohn was born in San Francisco, California, in 1883. He obtained the degrees of A.B. in 1905, and M.S. in 1907, from the University of California. He graduated from the Johns Hopkins University School of Medicine in 1911. On return to California he joined the staff of the Leland

Stanford, Jr., Medical School at San Francisco in 1912. Over a period of years he advanced to Clinical Professor of Medicine. He was attached to the staffs of the San Francisco Hospital and the Hospital for Women and Children as Neuropsychiatrist; to the staff of the Mount Zion Hospital, San Francisco, as consulting Neurologist.

In 1917 Dr. Wolfsohn entered the service of the U. S. Army Medical Corps in World War I, and was for a time stationed in London, England. After two years he returned to civilian life in San Francisco, taking up again his work in Neurology and Neuropsychiatry. He became consulting Neuropsychiatrist to the Veterans' Administration Facility at Fort Miley and the Alcatraz Penitentiary, San Francisco.

Dr. Wolfsohn was a diplomate of the American Board of Psychiatry and Neurology; a member of the San Francisco Medical Society, California State Medical Society and the California Academy of Medicine. In 1921 he became a Fellow of the American College of Physicians. Other memberships were:—Fellow of the American Medical Association and member of the San Francisco Neurological Society.

During the past few years prior to his death, Dr. Wolfsohn was forced to limit his professional activities owing to chronic illness. He is survived by his widow and two sons.

ERNEST H. FALCONER, M.D., F.A.C.P.,
Governor for Northern California

DR. ROBERT COPELAND MOONEY

Dr. Robert Copeland Mooney, Fellow of the American College of Physicians since 1931, died in Worcester, New York, on October 4, 1943, from cardiovascular disease after a five months' illness.

Dr. Mooney was born in Worcester, New York, on March 23, 1883. He was graduated from the Albany (New York) Medical College in 1908, following which he served an interneship in the Albany Memorial Hospital, continuing in postgraduate study at Harvard University and the Trudeau School of Tuberculosis. In 1910 he entered private practice at Speculator, New York, continuing there until 1916, when he moved to Gloversville, New York, and engaged in the general practice of medicine until 1918. He served as First Lieutenant, Medical Corps, United States Army, during World War I from 1918 to 1920. After his release from military service, he associated himself with the U. S. Public Health Service, later being transferred to the U. S. Veterans Bureau and Veterans Administration. From the beginning of his service in 1921 with the U. S. Public Health Service, he served at many stations, where his ability as a diagnostician was demonstrated. For several years prior to his death, he was a Senior Medical Consultant assigned to the Board of Veterans Appeals, Veterans Administration, Washington, D. C.

Dr. Mooney was a man of broad attainments and an ardent student, never tiring in his endeavor to keep in touch with modern medicine. His death is lamented by all who knew him.

CHARLES M. GRIFFITH, M.D., F.A.C.P.

DR. WALTER RALPH STEINER

Dr. Walter R. Steiner died at the Hartford Hospital, Hartford, Connecticut, November 5, 1942. His health had been failing for several years, and in the spring of 1942 he developed an epidural abscess with generalized staphylococcic sepsis. The abscess was drained and the sepsis was controlled by penicillin, but a series of cerebral thrombi ensued which finally proved fatal after an illness of five months.

Dr. Steiner was born November 18, 1870, in Frederick County, Maryland, a descendant of Jacob Steiner, a German immigrant who settled in Maryland early in the 18th Century. Steiner's father, Lewis Steiner, also a physician, spent most of his professional life as a teacher of Chemistry and Pharmacy and his latter years, as a librarian. Walter Steiner inherited his father's scholarly tastes and love of books. His mother, Sarah Spencer Smyth, was a native of Guilford, Connecticut, where Dr. Steiner spent many summers in his youth.

Walter Steiner received his academic training at Yale, obtaining his A.B. in 1892. After two years of graduate work in Chemistry and Biology at Johns Hopkins University, he entered the second class of the newly-established Hopkins Medical School, receiving his M.D. in 1898. Then followed a two year appointment as house officer in the Johns Hopkins Hospital, where he served under Osler, Halsted and Kelly. At the close of this interneship in 1900 he settled in Hartford.

Steiner's training and ability were early recognized in Hartford, and in 1901 he was appointed Pathologist and Bacteriologist to the Hartford Hospital. In 1905 he became also an Assistant Physician, and from 1908 to 1934 was an Attending Physician. As he became better known to the profession in Hartford and New Haven Counties, he received appointments as Consulting Physician to the Hartford Orphan Asylum, the Hartford Municipal Hospital, and the general hospitals in the neighboring cities of Meriden, Middletown, Manchester, New Britain, and Torrington.

Dr. Steiner was actively interested in both local and national medical societies. He took a lively interest in the affairs of the Hartford City, Hartford County, and Connecticut State Medical Societies. Of the last named he was Secretary from 1905 to 1912, Chairman of the Council from 1929 to 1933, and President in 1934–5. In all these capacities he exerted a pronounced influence on the policies of the Society. Dr. Steiner also represented Connecticut in the House of Delegates of the American Medical Association for many years and, in addition, was a member of the Associa-

tion of American Physicians, the Clinical and Climatological Association, the Medical Library Association, the American Association of the History of Medicine, and the Charaka and Beaumont Historical Clubs. He was for many years Secretary of the Congress of American Physicians and Surgeons.

Aside from his hospital and Medical Society activities, Walter Steiner's contributions to medicine were mainly along two lines: (1) his lifelong devotion to the library of the Hartford Medical Association, and (2) his contributions to medical literature.

As librarian to the Hartford Medical Society, he built up a collection of over 22,000 volumes, including complete files of the important medical journals. His labors were recognized by his colleagues who, during his lifetime, named the institution the Walter R. Steiner Library.

Dr. Steiner's most important writings were historical, and he was particularly interested in the early New England practitioners, both clerical and lay. He had a fund of information regarding these worthies and wrote, among others, of Elisha North, Elisha Perkins, Lemuel Hopkins, William Beaumont, and Nathan Strong. He published also several treatises for text books, and clinical articles on such varied subjects as venous thrombosis, dermatomyositis, hereditary hemorrhagic telangiectasia, focal and general infection, and diseases of the muscles.

In the death of Walter Steiner, the profession of the United States has lost an authority on some phases of medical history and of medical practice, and the people of Connecticut have lost an able, humane, and accomplished practitioner and a public servant of high ideals.

GEORGE BLUMER, M.D., F.A.C.P.

DR. WILLIAM HENRY LOHMAN

Dr. William Henry Lohman was born in West Orange, N. J., and died at his home in Brooklyn, N. Y., August 8, 1943. He received his medical degree at Columbia University College of Physicians and Surgeons in 1904 and spent the following year as resident pathologist and two years thereafter as intern at the Brooklyn Hospital. Most of Dr. Lohman's professional life was centered at the Brooklyn Hospital, where he rose to the rank of Chief Attending Physician in the year 1925, and continued to direct the Medical Division until his death. Earlier he spent a few years in the Outpatient Department of the Long Island College Hospital and taught Physical Diagnosis while he was there. In 1931 the Brooklyn Hospital became associated with the Long Island College of Medicine and Dr. Lohman was given the direction of the medical teaching with the rank of Professor of Clinical Medicine, a responsibility to which he gave much time and thought. In the meantime, he had given several years of service as Physician and Physician-in-Chief to the Brooklyn Thoracic Hospital. He was Consulting Physician to St. Johns Hospital and to the North Country Community Hospital in

Glen Cove, and for many years was a member of the Advisory Committee on Pneumonia Control, New York City Department of Health. During the First World War he served as Lieutenant in the U. S. Navy, serving as Chief of the Medical Service in Navy Base Hospital No. 1, Brest, France, and of the Camp Hospital No. 15, A.E.F. He was a member of the Kings County and New York State Medical Societies and was a Fellow of the American Medical Association, New York Academy of Medicine and the American College of Physicians (1937) and was a diplomate of the American Board of Internal Medicine.

Dr. Lohman was an accomplished internist, a wise and quiet gentleman, and a teacher whose influence will be felt for many years.

TASKER HOWARD, M.D., F.A.C.P.,
Brooklyn, N. Y.

DR. EDMUND PENDLETON SHELBY

Dr. Edmund Pendleton Shelby, F.A.C.P., Venice, Florida, died at Lexington, Kentucky, September 22, 1943, of carcinoma, at the age of 76.

Dr. Shelby was born November 26, 1866. He received his A.B. degree (1887) and his A.M. (1908), from the University of Kentucky. His medical training was received at New York University Medical College (1891). He interned at the Jersey City Hospital, 1891–92, and was later pathologist at the New York City Hospital. From 1897 to 1899, he was Director of the New York City Branch of the Loomis Sanatorium. From 1918 to 1934, he was Clinical Professor of Medicine at the University and Bellevue Hospital Medical College, New York City. He then removed to Venice, Florida, becoming Consultant in Medicine to the Florida Medical Center.

Dr. Shelby had been at one time President of the New York Pathological Society; also at one time Chairman of the Section on Medicine of the New York Academy of Medicine. He was a member of the Sarasota County Medical Society and Florida Medical Association. He was a Fellow of the American Medical Association, and had been a Fellow of the American College of Physicians since 1920.

ANNALS OF INTERNAL MEDICINE

PUBLISHED MONTHLY BY

The American College of Physicians

Publication Office: Prince and Lemon Sts., Lancaster, Pa.
Executive Office: 4200 Pine Street, Philadelphia, Pa.

VOL. 19 (O.S., Vol. XXIV) DECEMBER, 1943 NUMBER 6

CONTENTS

Subscription per volume or per annum, net postpaid, $7.00, United States, Canada, Mexico, Cuba, Canal Zone, Hawaii, Puerto Rico; $8.00, other countries.

Entered as Second Class Matter August 21, 1933, at the Post Office at Lancaster, Pa., under the Act of March 3, 1879. Acceptance for mailing at a special rate of postage provided for in the Act of February 28, 1925, embodied in paragraph 4, section 538, P. L. & R., authorized October 7, 1936.

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ANNALS OF INTERNAL MEDICINE

Official Periodical of the American College of Physicians

Place of Publication—Prince and Lemon Sts., Lancaster, Pa.

Editorial Office—University Hospital, Baltimore, Md.

Executive Office—4200 Pine Street, Philadelphia, Pa.

The Annals of Internal Medicine is published by the American College of Physicians. The contents consist of contributions in the field of internal medicine, editorials, book reviews, and a section devoted to the affairs of the College.

Manuscripts. All correspondence relating to the publication of papers and all books and monographs for review should be addressed to the editor. No manuscripts will be accepted without his consideration. Bibliographic references are to conform to the following style:

4. Doe, J. E.: What I know about it, Jr. Am. Med. Assoc., 1931, xcvi, 2006–2008.

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Lancaster Press, Inc., Lancaster, Pa.

Index photographed at the
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